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ADVANTAGES OF ADDING APPLE TO MILK FORMULAS

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Much work has been done by pediatricians and others in an effort to treat cow's milk so that it may be substituted more satisfactorily for breast milk. This work has been mainly in two fields.

The earlier efforts were aimed at raising the hydrogen ion concentration or reducing the buffering capacity. It is well known that digestion in the infant's stomach takes place at a p_H of 3 to 5, as compared with a p_H of about 2 in the adult. Owing to this fact it is important that the milk ingested have not too high a buffering value. Breast milk is ideal in this connection. Cow's milk and goat's milk, on the other hand, are comparatively resistant to a change in p_H. As has been pointed out many times, the main factor contributing to this discrepancy is the presence of larger quantities of protein in these milks. Several methods of destroying the buffer effect have been advocated. Marriott introduced lactic acid milk, Faber advocated hydrochloric acid milk and Dunham prescribed acetic acid milk. Hess added lemon juice to milk, thereby adding both citric acid and vitamin C. These acidified milks have been used satisfactorily for many years.

Brennemann was one of the first in this country to call attention to the importance of "soft curd" milks. It has been found that the curd tension of milk is proportional to the casein content. Soft curd milk can, then, be produced by merely diluting cow's milk. Again, a milk which has been treated with heat yields a soft curd. Goat's milk presents an interesting phenomenon. It has a high buffering value and contains a large amount of casein, yet it is well tolerated by most infants. This is thought to be due to the relatively high percentage of albumin, the colloidal nature of which makes for a soft curd. Furthermore, children feeding on goat's milk may avoid allergic reactions encountered with cow's milk.

In the course of our work with the apple we noted that it contains substances which should both raise the acidity and lower the curd tension of milk, that is, malic acid and pectin, respectively.

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EXPERIMENTAL PROCEDURE

Acid was added to the samples of milk, which were then stirred mechanically for about fifteen minutes. A Beckmann p_H meter was used to determine the p_H values. In each experiment 25 cc. of milk or milk mixture[1] was used, from

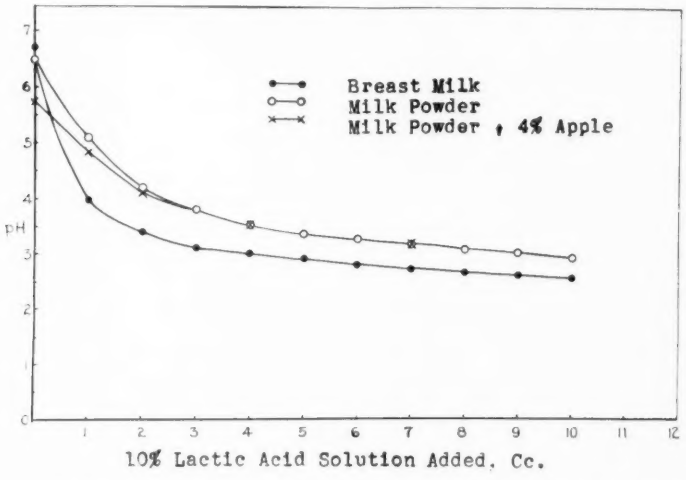

Fig. 1.—Buffer action. The chart shows the effect of the addition of lactic acid to various milks and milk mixtures.

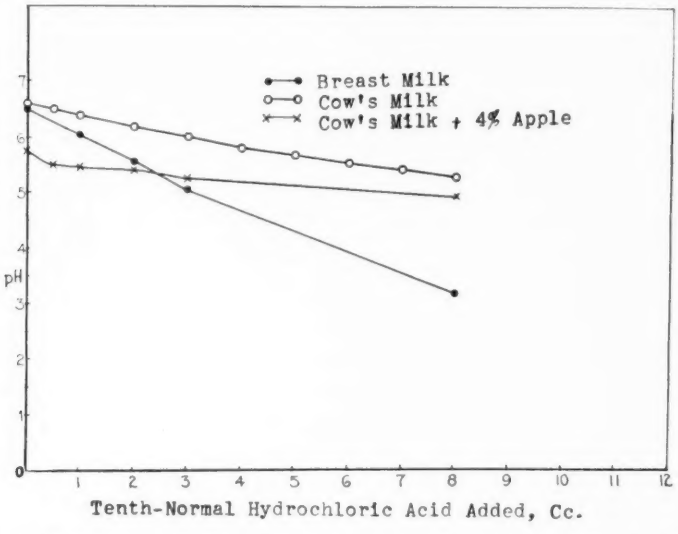

Fig. 2.—Buffer action. The chart shows the effect of the addition of hydrochloric acid to various milks and milk mixtures.

1. Milk to which was added 4, 5 and 6 per cent of apple in the dehydrated form.

which portions were taken for determination of p_H. Figure 1 shows the curves obtained by adding 10 per cent lactic acid to various milks. Figure 2 indicates results obtained with tenth-normal hydrochloric acid.

The addition of apple lowers the buffer index, $-\frac{dB}{dpH}$, somewhat. Its main value is that it lowers the initial p_H.

In the work on curd tension, test tubes were filled with the milk mixtures which were coagulated with rennin. Figure 3 indicates the results. It will be noticed that in the 4 per cent mixture the curd was flocculent and could be dispersed in the whey easily. The 5 per cent mixture showed less tendency to

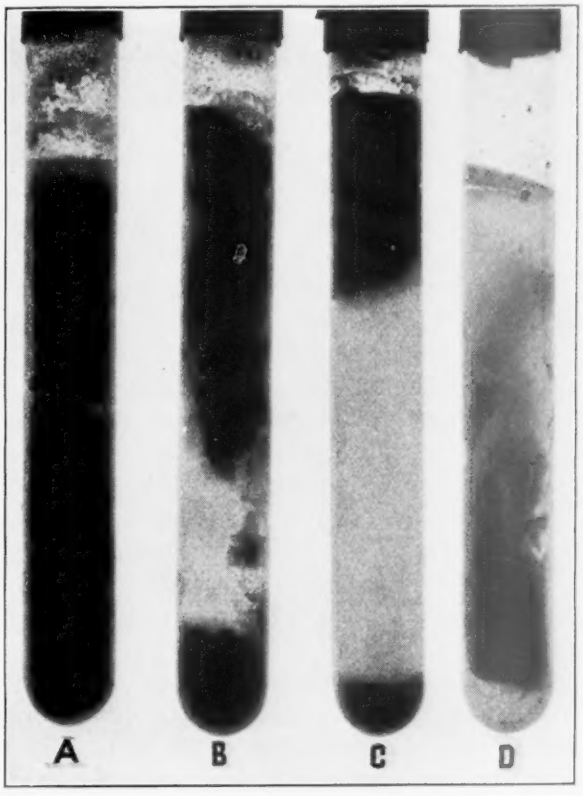

Fig. 3.—Milk mixtures coagulated by rennin. *A* indicates a mixture containing 6 per cent of dehydrated apple; *B*, a mixture containing 5 per cent of dehydrated apple; *C*, a mixture containing 4 per cent of dehydrated apple; *D*, a mixture to which no apple has been added.

separate, while the 6 per cent mixture separated very little. Evidently the pectin adsorbed the whey. In the 3 instances just cited the curd formed was fine, soft and fragile.

COMMENT

The earliest attempts to adjust cow's milk formulas to meet the digestive requirements of the infant were largely concerned with over-

coming the greater buffer value of cow's milk. Lactic acid seemed the obvious acid to use, since it is the acid occurring naturally in milk as it sours.

The use of hydrochloric acid, however, seems more physiologic, since this is the acid on which the body must depend for any reduction in the buffering ability of food material and in the creation of an optimal reaction for peptic digestion.

It will be noted in figure 1 that the maximum effect of 10 per cent lactic acid was accomplished by the addition of 3 cc. The p_H of the milk was reduced by such an addition from slightly less than 7 to slightly over 3. A further addition of 7 cc. accomplished little change in the p_H. In contrast to this, the addition of hydrochloric acid (figure 2) showed no indication of slacking off in its effect on the p_H even after 8 cc. had been added. The maximal effect of the addition of lactic acid is obtained when the milk is brought to a p_H of about 3.2. This is not true with hydrochloric acid; a greater reduction still may be accomplished, and with a much smaller amount of acid.

When dehydrated apple is added to a cow's milk formula the initial p_H of the formula is reduced from 6.5 to 5.7. Reduction in the buffer value of this formula by the addition of lactic acid is less effective than without the addition of apple. Nevertheless, the p_H is distinctly lower until a p_H of 3.9 is reached, when the effect of the apple, so far as its buffer value is concerned, is totally lost.

With hydrochloric acid, however, the addition of apple distinctly lowers the p_H throughout the entire range studied. In other words, with apple added to the milk formula, not only is the initial p_H lower but less hydrochloric acid is needed to bring the p_H down to a given point. The cow's milk formula is therefore definitely improved by such an addition.

While the addition of acid to a food is of distinct benefit in supplementing a possible gastric deficiency, it is of further and, perhaps, of greater value in its effect on the nature of the curd. With the addition of apple this effect is twofold. In the first place, the increased acidity of the compound produces a curd that is not only finer and softer but also more fragile and flocculent. Second, the colloidal nature of pectin keeps the curd in suspension and thus prevents the formation of a compact precipitate. In the flocculent form the curd is much more susceptible to the action of the digestive enzymes.

SUMMARY

This work indicates that the addition of apple to milk accomplishes two purposes—the p_H is lowered and a soft curd is produced. It seems advisable, then, to use such mixtures (4 to 5 per cent) in infant feeding in cases in which cow's milk is digested with difficulty. This finding is being confirmed by clinical observations.

PHLYCTENULOSIS

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The number of cases of phlyctenulosis in the United States has been rapidly decreasing since the World War. Redding [1] demonstrated this by diagrams showing the incidence of phlyctenular keratitis and conjunctivitis at the New York Eye and Ear Infirmary and at the Wills Hospital in Philadelphia. Similar statistics from Vienna had not shown a parallel decrease.

The annual average number of patients, both adults and children, in whose cases a diagnosis of phlyctenular disease was made at the Massachusetts Eye and Ear Infirmary is presented for five year periods from 1910 to 1934, and for the past two years, in table 1. The average annual number of cases observed in 1935 and 1936 was but 7.5 per cent of the annual number in the period from 1910 to 1914 and but 10 per cent of that in the period from 1915 to 1919. Statistics gathered by the state board of health revealed that the yearly morbidity from pulmonary tuberculosis in Massachusetts in 1935 and 1936 was 36.5 per cent of that observed from 1910 to 1914, and the death rate 32.5 per cent of that for the same period. The death rate from nonpulmonary tuberculosis in Massachusetts in 1935 and 1936 was 14.5 per cent of that observed from 1910 to 1914. The number of cases of tuberculous adenitis observed at the Massachusetts General Hospital shows an even greater decrease than does the number of cases of phlyctenulosis.

During the past fifteen years, data and observations regarding children with phlyctenulosis in the outpatient departments of the Massachusetts Eye and Ear Infirmary and the Massachusetts General Hospital have been systematically collected. Children in whose cases an ophthalmologist has made a clinical diagnosis of phlyctenular conjunctivitis or of phlyctenular keratitis have been referred to the children's outpatient department of the Massachusetts General Hospital for tuberculin tests, physical examinations, roentgen studies and general

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1. Redding, L. G.: Phlyctenular Disease and Vitamine Deficiency, Pennsylvania M. J. **39**:158 (Dec.) 1935.

medical observations. Data prior to 1929 were collected by the late Dr. Michele Nigro.

Table 2 shows the incidence of positive reactions to tuberculin tests in our series of 502 children for whom a diagnosis of phlyctenulosis was made. Three fifths of the patients were girls. A higher percentage of girls than of boys reacted positively to such tests.

In the Mantoux test, 0.1 cc. of a 1:1,000 dilution of old tuberculin (0.1 mg.) was used. If the reaction was negative with the 1:1,000

TABLE 1.—*Annual Incidence of Phlyctenulosis in Patients Treated at Massachusetts Eye and Ear Infirmary, as Compared with Incidence of Tuberculous Adenitis at Massachusetts General Hospital and with Rate of Morbidity and Mortality from Tuberculosis in Massachusetts*

		State of Massachusetts			
Period	M. E. & E. I., Phlyctenulosis	Pulmonary Morbidity	Death from Tuberculosis	Death from Nonpulmonary Tuberculosis	M. G. H., Tuberculous Adenitis
1910-1914	384	211	123	24.4	...
1915-1919	281	208	119	23.0	258
1920-1924	259	146	81	15.2	149
1925-1929	144	121	66	11.2	84
1930-1934	54	94	50	5.8	19
1935	31	82	42	3.4	2
1936	26	73	39	3.7	13

TABLE 2.—*Phlyctenulosis in Children—Incidence of Positive Reaction to Tuberculin Tests*

	Total Number of Patients	Positive Reaction	Percentage of Positive Reactions
Boys	203	114	56.1
Girls	299	186	62.3
1921-1928—Pirquet	195	109	55.8
1929-1936—Mantoux	307	191	62.2
Total	502	300	59.7

dilution, a test with a 1:100 dilution was made as a matter of routine (since 1933). In no instance did the stronger concentration of tuberculin produce a positive reaction.

In our patients with phlyctenulosis, when the reaction was positive it was almost invariably strongly positive; it was not unusual for the reaction to be so intense that ulceration followed. Therefore, in testing patients with phlyctenulosis, we now recommend that a 1:10,000 dilution be used.

The incidence of positive reactions to tuberculin tests among children of different ages with phlyctenulosis is shown in table 3. The child's age at the time of the first attack was used. In a number of instances this information was not available, so that the data on only 437 of the 502 children are given.

No consistent relation between the ages of the children and the percentage of positive reactions to tuberculin tests is apparent to us from this table.

In the last column of the table are given the expected percentages of children of each age group reacting positively to tuberculin tests. A child with phlyctenules is much more likely to react positively than is another child of the same age.

A tuberculin test is known to elicit a negative reaction in some tuberculous children who have recently been infected (even as long before as six months) or who have overwhelming infections or who have temporary anergy resulting from measles, influenza or possibly some

TABLE 3.—*Incidence of Positive Reactions to Tuberculin Tests in Relation to the Age of the Patient at the Onset of Phlyctenulosis*

Age	Patients	Positive Reaction	Percentage of Positive Reactions	Expected Percentage of Positive Reactions*
Under 2	35	23	65.7	10
2	72	43	59.7	13
3	47	30	63.8	17
4	38	15	39.4	20
5	44	24	54.5	21
6	36	21	58.3	20
7	46	22	47.8	22
8	35	21	60.0	23
9	26	15	57.6	24
10	22	14	63.6	28
11	19	14	73.1	29
12	8	4	50.0	30
13	8	7	87.5	34
14	1	0	0	33

* Dickey, L. B., and Seitz, R. P.: Am. Rev. Tubere. **23**: 13 (Jan.) 1931 (children under 4 years of age).
Chadwick, H. D., and Zacks, D.: New England J. Med. **200**: 332 (Feb. 14) 1929 (children above 4 years of age).

other acute infection. Also, some persons who react positively to tuberculin may eventually become desensitized. Therefore, the tuberculin tests were repeated for 35 of our patients; for 3 after six months, for 6 after one year, for 12 between two and five years and for 14 between six and nine years. Twenty-four gave positive reactions on the first test, and 11 gave negative reactions; the reactions of the same 24 were positive and those of the same 11 negative in the subsequent test.

Table 4 gives data on the incidence of positive reactions to tuberculin tests in the patients for whom a diagnosis of phlyctenular keratitis or conjunctivitis was made by each of eleven of the more experienced members of the ophthalmologic staff of the Eye and Ear Infirmary. The percentage of positive reactions varied from 43 (Dr. C.) to 90 (Dr. F.). Dr. I., who found 46 per cent of positive reactions, had done

considerable investigative work on phlyctenulosis. None of the physicians found so high a percentage as that reported by Goldstein and Wood [2] (96.6).

It appears that there is probably some variation in the clinical criteria used by ophthalmologists as to what constitutes phlyctenular disease; but all ophthalmologists have observed cases in which the tuberculin test produced negative reactions.

In our series, only those patients for whom a positive diagnosis was made were included. If subsequent data or observations revealed the

TABLE 4.—*Percentage of Positive Reactions to Tuberculin Tests in Cases of Phlyctenulosis Observed by Different Ophthalmologists*

Diagnostician	Patients	Positive Reaction	Percentage of Positive Reactions
Dr. A	5	4	80
B	6	4	66
C	7	3	43
D	8	4	50
E	9	7	77
F	10	9	90
G	12	9	75
H	13	7	54
I	15	7	46
J	16	9	56
K	26	13	50

TABLE 5.—*History and Clinical Signs of Tuberculosis in Patients with Phlyctenulosis*

	Total Number of Patients	Positive Reactions	Negative Reaction
	502	300	202
Family history of tuberculosis	109 (22%)	79 (26%)	30 (15%)
Clinical tuberculosis	109 (22%)	109* (36%)	0 (0%)

* Distributed as follows:

Tuberculosis of the hilus	94
Tuberculosis of other glands	11
Peritonitis (and meningitis)	2
Dactylitis	1
Tuberculous pneumonia (epituberculosis)	1

first diagnosis of phlyctenulosis to be incorrect, the patient was excluded. Patients were included or excluded, however, on a clinical basis, without regard to the results of the tuberculin test.

For clinical diagnosis, a roentgenogram of the chest was taken of each patient for whom a diagnosis of phlyctenulosis had been made. It was a coincidence that the same number of patients had a family history of tuberculosis as gave clinical or roentgenologic evidence of tuberculosis; they were not, however, invariably the same patients. The

2. Goldstein, M., and Wood, C. L.: Tuberculosis: Phlyctenular Conjunctivitis: Its Relation to Tuberculosis as Shown by Roentgenologic and Clinical Observations in Seventy-One Cases, Am. J. Dis. Child. **47**:171 (Jan.) 1934.

clinical manifestations, as listed in table 5, were usually symptoms of primary, or "childhood," tuberculosis, and, consequently were not immediately serious. Only 3 patients were critically ill with tuberculosis.

The data on the body weight of the children with phlyctenulosis indicate that quite as many children were overweight as were underweight, both in the groups with positive and in those with negative reactions to the tuberculin test. The patients 5, 6 and 7 years old tended to be underweight, and those 10, 11 and 12 years old tended to be overweight.

TABLE 6.—*Relative Body Weight of Children with Phlyctenular Conjunctivitis and Keratitis*

				Underweight			Overweight	
	Age Group	Total	No Record of Weight	10%+	5% to 10%	Normal	5% to 10%	10%+
Positive Reaction to Tuberculin Test								
1929-1933	Under 5	61	13	12	7	11	8	10
	5, 6, 7	32	3	9	6	8	1	5
	8, 9	19	1	2	1	5	6	4
	10, 11, 12	21	1	4	2	1	3	10
		133	18	27	16	25	18	29
1921-1928		109	0	27		61		21
Negative Reaction to Tuberculin Test								
1929-1933	Under 5	24	1	6	2	8	2	5
	5, 6, 7	23	1	6	5	4	1	6
	8, 9	11	0	3	0	0	3	5
	10, 11, 12	9	0	3	0	2	0	4
		67	2	18	7	14	6	20
1921-1928		86	4	15		49		18

COMMENT

Aland,[3] in 1925, in reviewing the etiology and pathology of phlyctenular keratoconjunctivitis, listed nine theoretical causes of that condition which have been presented. There is clinical and circumstantial evidence in favor of each, but absolute proof is missing. Aland's list is as follows:

1. Bacterial infection (bacteria actually in the lesions)
2. Intestinal intoxication
3. Tuberculosis
4. One-sided carbohydrate diet
5. Diseased state of the mucous membranes (especially nose, throat or sinuses)
6. Eczema
7. Exanthem
8. Pediculosis capitis
9. Chronic ethmoiditis with obstruction

3. Aland, A. H.: Etiology and Pathology of Phlyctenular Keratoconjunctivitis, Am. J. Ophth **8**:948 (Dec.) 1925.

More recently, Redding [1] has argued that deficiency in vitamin A is the cause of phlyctenulosis.

In summary, we may classify these possible causes under four main headings:

1. Diet
2. Infection
3. Allergy
4. Local irritants

Under the classification of diet should be included deficiency in vitamins, malnutrition, indigestion and specific foods. The infection may be focal, toxic or allergic; it may be tuberculous or nontuberculous. Sequelae of infections must also be considered. Under the heading of allergy one must consider the various antigens, such as foods, pollens, dust and bacteria, and also the manifestations or sequelae of eczema and urticaria. Under the heading of irritations should be included foreign substances in the eye, such as insects or poisons.

Interrelations between these four possible causes are obvious. Thus, a local irritant may be allergic, or a dietary deficiency may be accompanied by infection. The study of possible causes raises the question whether phlyctenulosis is a definite pathologic condition arising from a simple and definite cause or whether it includes similar pathologic conditions arising from similar (or even dissimilar) causes. One can realize the difficulty of determining the cause when one considers that the diagnosis of phlyctenulosis must be made on the history and clinical appearance of the lesion. The diagnosis certainly cannot be regarded as absolutely precise and is probably not strictly accurate differentially. The confusion of ideas as to the cause of this condition is probably the result of the inadequacy of its differential diagnosis.

At this point, it seems feasible to review the clinical relationship of phlyctenulosis and tuberculosis. The word "phlyctenule" comes from the Greek word φλύκταινα, meaning bladder. In phlyctenulosis, phlyctenules are seen on the cornea or on the conjunctiva and are usually about the size of a millet seed. They are gray or pinkish and are surrounded by vascular engorgement. Histologically, phlyctenules consist of epithelioid cells, polymorphonuclear leukocytes and lymphocytes; tubercle bacilli are not present, nor are the giant cells which one is accustomed to find in a tubercle.

For more than one hundred years phlyctenulosis has been generally associated with the scrofulous patient; in fact, it has been called "scrofulous ophthalmia." With the clinical application of tuberculin tests (and especially of the Pirquet test, which was first described in 1907), the relation between scrofula and tuberculosis was established, and observations on the frequency of positive reactions to tuberculin tests in patients with phlyctenulosis began to appear in the literature.

In 1910, a committee of the Section on Ophthalmology of the American Medical Association [4] reported that of 51 patients with phlyctenular disease of the cornea or the conjunctiva 47 showed distinct evidence of the presence of tuberculosis. In 1918, Gibson [5] collected reports of 903 cases of phlyctenulosis from the literature; the Pirquet reaction was positive in 769 patients, or 85 per cent. Carvill [6] in 1929 reported a positive Pirquet reaction in 71.7 per cent of 234 children from 1 to 14 years of age. Goldstein and Wood [2] in 1934 reported positive reactions to the tuberculin test in 96.6 per cent of 60 patients with phlyctenulosis. The percentages of positive reactions reported have varied from about 60 to 100 in cases of phlyctenulosis. The variation in these figures is doubtless to be based on the question of clinical diagnosis of the ocular lesion. One wonders whether some clinicians may not have hesitated to make a diagnosis of phlyctenulosis without a positive reaction to the tuberculin test.

Casparis [7] in 1927 expressed the opinion that phlyctenulosis is due to a local sensitization of the eyes to tuberculosis. The more recent tendency has been to explain phlyctenules as an allergic reaction of the sensitized epithelial surface of the cornea and/or the conjunctiva. This explanation is well reviewed by Woods in his book on "Allergy and Immunity in Ophthalmology" [8]. In favor of this explanation is presented the fact that instillation of tuberculin into the conjunctiva frequently causes the appearance of phlyctenules. Also, Loddoni [9] has shown that similar phlyctenules are seen in animals sensitive to horse serum when horse serum is injected into the conjunctival sac. Lemoine [10] has reported 2 cases of phlyctenular keratitis apparently due to hypersensitivity to strawberries and face powder respectively. If one is to accept this explanation of phlyctenulosis, one would expect the patients either to be sensitive to tuberculin (and probably extremely so) or to be sensitive to some other allergen.

At present, the explanation of phlyctenulosis on an allergic basis seems the most probable theory as to its cause, especially so far as hyper-

4. Wilder, W. H.: Report of the Committee for the Study of the Relation of Tuberculosis to Diseases of the Eye, J. A. M. A. **55**:21 (July 2) 1910.

5. Gibson, W. S.: Phlyctenular Conjunctivitis, Am. J. Dis. Child. **15**:81 (Feb.) 1918.

6. Carvill, M.: A Contribution to the Study of Phlyctenular Keratoconjunctivitis, Tr. Am. Ophth. Soc. **27**:314, 1929.

7. Casparis, H.: Phlyctenular Kerato-Conjunctivitis: Its Etiology and Treatment, Am. J. Dis. Child. **34**:779 (Nov.) 1927.

8. Woods, Alan C.: Allergy and Immunity in Ophthalmology, Baltimore, Johns Hopkins Press, 1933.

9. Loddoni, G.: Cherato-congiuntivite flittenulare e allergia, Ann. di ottal. e clin. ocul. **58**:28 (Jan.) 1930.

10. Lemoine, A. N.: Ocular Anaphylaxis, Arch. Ophth. **1**:706 (June) 1929.

sensitivity to tuberculin is concerned. Our observation that the reactions to tuberculin tests if positive were strongly positive is certainly evidence that the patients in our series were hypersensitive to tuberculin. Our data on nutrition and on clinical evidence of tuberculosis fit in with the observation of Casparis [7] that "One rarely sees phlyctenulosis in a tuberculous patient that is doing badly" and furnishes further argument that the appearance of phlyctenules is a manifestation of hypersensitivity to tuberculoprotein. The decrease in the incidence of phlyctenulosis, as shown by our statistics, is greater than the decrease in the incidence of pulmonary tuberculosis; it approximates more nearly the decrease in the number of cases of surgical tuberculosis. Surgical tuberculosis is usually of bovine origin; the milk in the Boston area is pasteurized now and is obtained from tuberculin-tested animals. For the explanation of phlyctenulosis by the allergic theory, two factors must be present: (1) The patient must have become sensitized, and (2) the sensitized patient's eyes must have come in contact with tubercle bacilli. The proportion of sensitized children has decreased almost one third since 1910. The principal infecting agent reaching the eye seems to be dust. The amount of dust containing tubercle bacilli must have diminished with the decrease in the number of tuberculous patients, with the better hygienic conditions which are maintained and with the lessening of the amount of dust of all kinds in the community (the roads being now generally hard surfaced and containing much less animal manure).

Goldstein and Wood [2] reported: "It is possible that there is a relatively uncommon form of conjunctivitis clinically difficult at the onset to distinguish from tuberculous phlyctenulosis." Our observations would seem to modify "relatively uncommon" to "relatively common." We have tested 10 such patients for sensitivity to other allergens; none reacted positively to the common allergens—foods, animal allergens (hair and feathers) and pollens. We can say definitely that nontuberculous phlyctenulosis is not limited to the strikingly allergic person. Further study along this line should be made.

The allergen, if such is the responsible factor, seems to act slowly, as does tuberculin, and not rapidly, as do pollens, foods, and animal allergens.

SUMMARY

The yearly incidence of phlyctenulosis in 1935 and 1936 was, according to hospital statistics in Boston, but 7.5 per cent of that twenty-five years previously. The decrease is greater than the decrease in the annual incidence of pulmonary tuberculosis; it more nearly approximates that in the incidence of nonpulmonary tuberculosis.

Of 502 children for whom a clinical diagnosis of phlyctenulosis was made, 300 gave positive reactions to the tuberculin test. One hundred

and nine showed clinical or roentgenologic evidence of tuberculosis. In all of these the tuberculosis was of the primary or "childhood" type, and in all but 3 cases the condition was relatively mild.

Girls seem more likely to have phlyctenulosis than do boys.

The nutritional condition of the children with phlyctenulosis as a group was normal.

There is considerable evidence in our data that a phlyctenule is an allergic manifestation in the patient whose reaction to tuberculin is positive; for the reaction when positive is strongly positive, phlyctenules have not been observed in anergic tuberculous patients, and phlyctenules are rarely seen in the very sick tuberculous patient.

There is no evidence in our data that a phlyctenule is an allergic manifestation in the patient whose reaction to tuberculin is negative; in fact, such patients are usually not extremely atopic.

Phlyctenulosis should probably be divided into two types, the tuberculous and the nontuberculous. Clinical diagnosis, without a tuberculin test, is insufficient at present for differentiation between these two types. The cause of the nontuberculous type of phlyctenulosis has not been satisfactorily explained.

CHRONIC GAUCHER'S DISEASE

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Although a large number of cases of Gaucher's disease have been reported and many excellent discussions have appeared [1] concerning the primary diseases of lipid metabolism, which include Gaucher's disease, Hand-Schüller-Christian disease and Niemann-Pick disease, studies of two Negro siblings are presented here. These patients had the changes of Gaucher's disease in the spleen, liver, lymph nodes, blood, bone marrow and conjunctiva.

REPORT OF CASES

CASE 1.—Marshall L., a boy aged 7 years, was first admitted to Duke Hospital on July 7, 1936, with the complaint of having had a large stomach for the past three or four years. His sister Mary, aged 9 years, was admitted at the same time with a similar complaint. The father, aged 29 years, and the mother, aged 30 years, were living and well. There had been one other pregnancy, ending in a miscarriage at three months. The family history was otherwise noncontributory.

The boy had an uneventful history until the age of 4 years, when he began to have generalized convulsions, characterized by limpness of the neck and jerking of the entire body. There were no preceding auras, biting of the tongue or foaming at the mouth. These attacks occurred over a period of about three months, as frequently as fifteen times daily; then they subsided, disappeared spontaneously and did not recur.

At about the same time (the boy was 4 years of age) a small mass about 4 by 5 cm. was noted in the left upper quadrant of the abdomen, just below the costal margin. Since then the mass had grown steadily until it filled the entire abdomen. There had been no associated pain, nausea, vomiting, bloody diarrhea or hematuria. Two weeks prior to his admission the child's ankles began to swell, but the edema subsided after a few days. On the day before admission he fell and bruised his left eye. Except for slight weakness, he had apparently been feeling well and ate and slept regularly.

From the Department of Pediatrics, Duke University School of Medicine and Duke Hospital, Durham, N. C. This paper was completed at the time the author was a member of the Pediatric Staff, University of Chicago.

1. (*a*) Hoffman, S. J., and Makler, M. I.: Gaucher's Disease: Review of the Literature and Report of a Case Diagnosed from Section of an Inguinal Lymph Gland, Am. J. Dis. Child. **38**:775 (Oct.) 1929. (*b*) Reiss, O., and Kato, K.: Gaucher's Disease: A Clinical Study with Special Reference to the Roentgenography of Bones, ibid. **43**:365 (Feb.) 1932. (*c*) Rowland, R. S., in Brennemann, J.: Practice of Pediatrics, Hagerstown, Md., W. F. Prior Company, Inc., 1937, vol. 3, chap. 23, p. 15.

Physical examination showed an undernourished and poorly developed Negro boy who appeared cheerful (fig. 1). The mucous membranes were pale. The lymph glands, especially those in the axillary and inguinal regions, were enlarged. There was marked chemosis of the left eye, with evidence of fresh hemorrhage in the conjunctiva. Slight yellowish thickening of the conjunctiva of the right eye was visible at the corneoscleral margins of both temporal and nasal sides (fig. 2).

A rachitic rosary was present. Expansion of the chest was limited; the percussion note was hyperresonant above the eighth ribs posteriorly and dull at the bases of the lungs. Breath sounds were suppressed at both bases, and tubular breathing, with an occasional crepitant rale, could be heard. A systolic murmur was present throughout the entire left side of the precordium.

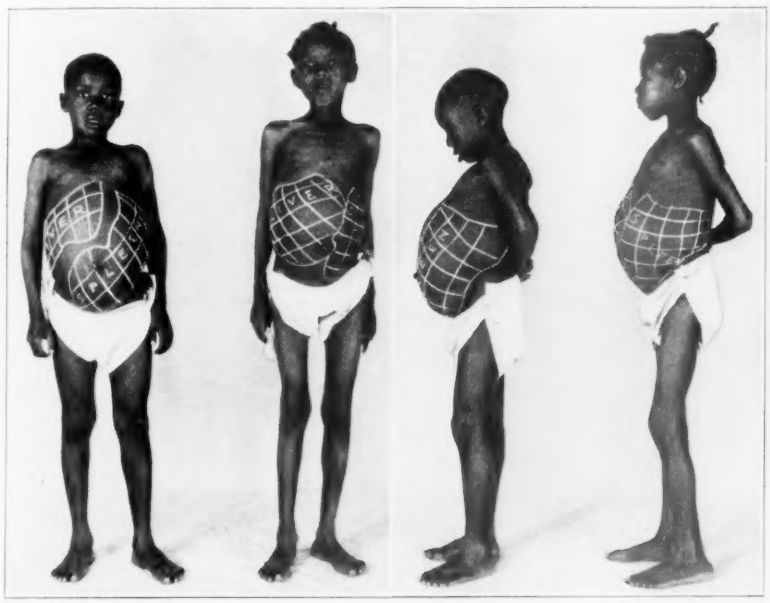

Fig. 1.—Photographs of the patients on their second admission (March 5, 1937), showing tremendous enlargement of the spleens and livers.

The abdomen was extremely protuberant, and the percussion note was flat. No ascites was demonstrable. The spleen was tremendously enlarged, the lower pole resting at the symphysis pubis and the notch being plainly visible at the umbilicus. The liver extended 9 cm. below the costal margin. The edges of both liver and spleen were smooth, firm and nontender. There was no edema of the lower extremities. The neurologic examination gave entirely negative findings.

Accessory clinical findings were as follows: Red blood cells numbered 3,600,000 per cubic millimeter; the hemoglobin content was 7.2 Gm. (46 per cent); white blood cells numbered 4,000, with polymorphonuclears 30 per cent, eosinophils 3 per cent, basophils 1 per cent, large lymphocytes 3 per cent and small lymphocytes 50 per cent. The platelet count was 192,000. The bleeding and coagulation

times were normal, and the Rumpel-Leede (tourniquet) test gave a negative result. Examinations of the urine and stool showed nothing abnormal. Results of Wassermann, Takata-Ara, galactose tolerance and tuberculin tests were negative. The Schick test gave a faintly positive reaction.

The patient was given two transfusions of citrated blood, the amounts totaling 300 cc., after which the hemoglobin concentration rose to 10.1 Gm. (65 per cent). A biopsy of an axillary node showed the lymphatic sinuses to be filled with large cells which took the eosin stain (fig. 3). Each of these cells had a fibrillar-appearing cytoplasm and one or more eccentrically placed nuclei. A large amount of brown pigment not stained blue by potassium ferrocyanide could be seen within many reticuloendothelial cells, usually within the sinuses but also within lymphoid tissue. No pigment could be demonstrated within the Gaucher cells. A fat stain with scarlet red failed to color the Gaucher cells red.

Fig. 2 (case 1).—Drawing of the right eye, showing the thickening of the conjunctiva at the corneoscleral margins.

Roentgenograms of the pelvis and long bones showed diffuse decalcification with small areas of destruction in the necks of both femurs (fig. 4).

The patient remained in the hospital for six weeks. The hemoglobin content increased, but no other changes were noted. Various studies were done on blood, urine and metabolism, a low fat diet was given, and the boy was discharged.

Seven months later, on March 5, 1937, the child returned to the hospital for further studies. During the interim nothing unusual had happened. Physical examination gave essentially the same findings as on the previous admission. The size of the spleen and of the liver appeared to have remained stationary. Roentgenograms of the long bones showed little change. On March 24, nineteen days after admission, the patient was discharged.

He was admitted on May 17 for biopsy of a lymph node and tissue culture. These studies were done, and he left the hospital a few days later.

Fig. 3 (case 1).—Photomicrograph (low power) of an axillary lymph node. The lymphatic sinuses are filled with large pale Gaucher cells, each of which has one or more eccentrically placed nuclei.

CASE 2.—Mary L., aged 9 years, who also complained of a large stomach, was admitted to Duke Hospital at the same time as her brother, Marshall. At the age of 5 years her abdomen began to increase in size and since then had become progressively larger. About ten months before her admission her parents noted a definite limp and beginning shortening of the right lower extremity. There had been no history of trauma.

Physical examination revealed an emaciated Negro girl whose abdomen was enormous (fig. 1). The skin and mucous membranes were very pale. A rachitic rosary and Harrison's groove were present. No ascites was demonstrable. The spleen and liver were greatly enlarged. The edges of these organs were smooth and nontender. There was elevation of the right greater trochanter with noticeable shortening of the right leg.

Fig. 4 (case 1).—Roentgenogram (July 8, 1936) of the pelvis and upper parts of the femurs, showing diffuse decalcification of the bones.

Accessory clinical findings were as follows: Red blood cells numbered 3,500,000 per cubic millimeter; the hemoglobin content was 6.8 Gm. (44 per cent); white blood cells numbered 3,560, with polymorphonuclears 48 per cent, large lymphocytes 18 per cent, small lymphocytes 32 per cent and monocytes 2 per cent. The platelet count was 310,000. The bleeding and coagulation times were normal. The tourniquet test gave a negative result. Reactions of Wassermann, galactose tolerance and Takata-Ara tests were also negative.

The patient was given a total of 525 cc. of citrated blood by numerous small transfusions, and her hemoglobin content rose to 10.5 Gm. (69 per cent). On her sixth day in the hospital a course of roentgen therapy was started, the girl receiving in five days a total of 250 roentgen units on each side in divided doses of 50 units. There was no change in the size of the spleen or liver. Roentgenograms of the thorax, shoulder girdle, pelvis and extremities showed extreme

decalcification of all the bones, thinning of the cortex and a pathologic fracture through the neck of the right femur. The cortex of both femurs was extremely involved, and numerous areas of destruction or absorption were present. The right acetabulum was irregular, with rather large areas of destruction, especially along the margin of the ilium (fig. 5 *A*).

Chemical and metabolic studies were also made, and the patient was given a low fat diet. She was discharged with her brother on August 20. There had been noticeable improvement in her general condition during her stay in the hospital. On discharge she appeared much stronger and was able to walk better, although the limp was unchanged.

She returned on two subsequent occasions (March 5 and May 17, 1937) and served as a control for studies done on her brother. Repeated roentgenograms showed progressive decalcification of all the bones, with increase in the angulation of the neck of the right femur (fig. 5 *B*). On May 18, the day following her last admission, she had a temperature of 39.3 C. (103 F.) and general malaise. This

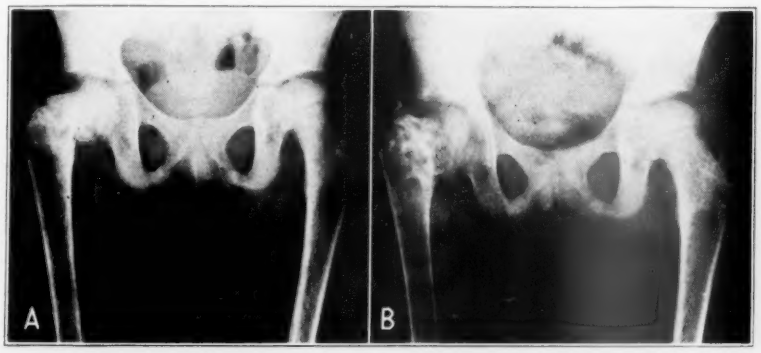

Fig. 5 (case 2).—*A*, roentgenogram of the pelvis and upper parts of the femurs, showing extreme decalcification of the bones and a pathologic fracture through the surgical neck of the right femur. *B*, roentgenogram taken ten months later, showing progressive decalcification of all the bones and increase in the angulation of the right femoral neck.

was followed a few days later by swelling of both parotid glands and inflammation of the orifices of Stensen's ducts. A diagnosis of epidemic parotitis was made, and the girl was discharged.

COMMENT

The familial incidence of the disease, the gradual onset, the painless enlargement of the spleen and liver, the involvement of the bones and lymph nodes and the changes in the conjunctivas are all consistent with the diagnosis of chronic Gaucher's disease.

About one third of the reported cases have occurred in two or more members of one family. The disease, however, has been found in different generations of the same family.[2] As in Niemann-Pick disease,

2. (*a*) Bloem, T. F.; Groen, J., and Postma, C.: Gaucher's Disease, Quart. J. Med. **5**:517, 1936. (*b*) Anderson, J. P.: Hereditary Gaucher's Disease, J. A. M. A. **101**:979 (Sept. 23) 1933.

a related disturbance of lipid metabolism, Gaucher's disease shows a predilection for Jews.[3] The disease also has been reported in other races. Three cases in a Japanese family have been described [1b] and 1 case in a 9 year old Negro boy.[1a]

The origin of the Gaucher cell is a matter of controversy. Histologic examination of tissues infiltrated with Gaucher cells has been carefully done by Pick [4] and by Mandlebaum and Downey.[5] The results of their studies favor the theory that the Gaucher cell originates ". . . from the reticulum of the spleen, lymph nodes and bone marrow, from the adventitial cells of the small arterioles of the splenic pulp and lymph nodes, and in the liver from the histiocytes of Glisson's capsule, as well as the adventitial and periadventitial connective tissue of smaller vessels and the central lobular veins." However, many believe that these abnormal cells arise from endothelial cells or from both reticulum and endothelial cells.[6]

Hepatomegaly and splenomegaly are outstanding physical signs of the disease. The enlargement is painless, but it results in considerable discomfort due to the weight of the involved organs and to the displacement of intra-abdominal and thoracic viscera.

The osseous changes which occur in Gaucher's disease have been discussed extensively by Reiss and Kato.[1b] The fusiform expansion of the lower ends of the femurs which has been considered pathognomonic of Gaucher's disease was not found in the cases presented here. However, generalized osteoporosis and rarefaction of the bones, a more constant finding in cases of the disease, were present. The upper ends of the femurs were extensively involved, and as a result a pathologic fracture through the surgical neck of the right femur occurred in one of the children (Mary).

Bone marrow obtained by punctures through the sternal plate contained the typical Gaucher cell, which was characterized by its huge size, by a hyperchromatic nucleus, usually eccentrically placed, and by finely granular cytoplasmic material, aggregated in strands and streaks (fig. 6).[7] Splenic punctures were not performed, as this procedure was thought unnecessary and somewhat hazardous, owing to the tremendous enlargement of the organ in both cases.

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3. Pick, L.: Niemann-Pick's Disease and Other Forms of So-Called Xanthomatosis, Am. J. M. Sc. **185**:601, 1933.

4. Pick, L.: A Classification of the Diseases of Lipoid Metabolism and Gaucher's Disease, Am. J. M. Sc. **185**:453, 1933.

5. Mandlebaum, F. S., and Downey, H.: The Histopathology and Biology of Gaucher's Disease (Large-Cell) Splenomegaly, Folia haemat. **20**:139, 1915-1916.

6. Rowland.[1c] Mandlebaum and Downey.[5]

7. Dr. Katsuji Kato of the Department of Pediatrics, University of Chicago, furnished the drawing and interpretation of the bone marrow smears.

Hypochromic anemia and leukopenia are usually present with this disease. Leukocytosis may occur.[8] Thrombopenia also has been a frequent finding, although a normal platelet count and thrombocythemia [1b] have been reported. The platelet counts in both these children were normal at various periods, and there was no history of a hemorrhagic diathesis in either case. Both children had hypochromic anemia. The white blood cell counts were never above 4,600, and there was a slight preponderance of polymorphonuclear cells (table 1). No abnormal cells were seen on blood smears (Wilson's stain). With the exception

TABLE 1.—*Differential Count of White Blood Cells*

Date	White Blood Cells	Polymorphonuclears, Percentage	Eosinophils, Percentage	Basophils, Percentage	Large Lymphocytes, Percentage	Small Lymphocytes, Percentage	Monocytes, Percentage
			Marshall L.				
7/ 7/36	4,000	30	3	1	3	50	0
8/16/36	4,000	54	0	0	6	40	0
3/ 5/37	3,800	54	4	0	22	20	0
3/ 6/37	3,400	62	2	0	20	16	0
3/ 8/37	3,800	54	2	0	20	24	0
3/ 9/37	3,400	41	6	0	16	35	0
3/11/37	3,800	50	1	0	10	39	0
3/13/37	3,780	46	2	0	20	32	0
3/15/37	3,200	40	4	0	20	36	2
3/17/37	3,600	50	4	0	22	22	2
3/19/37	3,400	38	2	2	18	40	0
3/23/37	3,500	56	1	0	7	36	0
5/17/37	4,600	36	6	1	6	48	5
5/20/37	4,200	57	0	0	7	31	4
5/22/37	4,300	60	3	0	6	25	5
			Mary L.				
7/ 7/36	3,560	48	0	0	18	32	2
7/19/36	3,880	60	2	1	14	20	3
7/26/36	2,200	52	1	0	15	30	2
3/ 5/37	2,200	40	0	0	12	44	4
3/ 6/37	2,050	52	0	0	7	40	1
3/ 8/37	3,200	48	0	0	10	40	2
3/ 9/37	2,800	50	0	0	12	38	0
3/10/37	3,150	52	0	0	8	50	2
3/14/37	2,900	50	0	0	14	36	0
3/16/37	2,100	42	0	0	14	38	6
3/19/37	2,200	40	0	0	16	40	4
3/23/37	3,000	56	0	0	6	38	0
5/17/37	3,000	62	0	1	5	30	2
5/20/37	2,600	48	3	2	19	19	9

of 1 case reported by DiGuglielmo,[8a] Gaucher's cells have never been demonstrated in the peripheral blood stream. The vacuolated white blood cells which are found in the blood stream in Neimann-Pick disease were consistently lacking.

Wedge-shaped, pinguecula-like thickening of the conjuntiva at the corneal margin occurs frequently in adults, but it is considered rare in infants and young children. Definite, pale yellow deposits were visible

8. Rinzer, N., in discussion on Anderson.[2b]

8a. DiGuglielmo, G.: Gaucher Cells in the Peripheral Blood, Haematologica **12**:615, 1931.

in the conjunctivas of both eyes of the boy (fig. 2), but could not be seen in the conjunctivas of his sister.

Although the disease has been diagnosed by biopsy of a node,[1a] the peripheral lymph nodes are not usually enlarged. Mary did not have any enlargement of lymph nodes, but the axillary and inguinal nodes of her brother were definitely enlarged. Biopsy of these nodes showed diffuse infiltration of Gaucher cells in both these regions.

Cultures of the tissue of inguinal nodes from the boy were done in the hope of throwing some light on the pathogenesis of this disease. A lymph node was removed and cut into two portions. One was fixed in Helley's fluid, sectioned and stained with Kingsley's blood stain; the other was cut into small fragments and cultured. Each fragment was planted in equal parts of chicken plasma and fresh juice of chick embryos. After incubation at 37 C. for seven days, three of fifty cultures gave evidence of growth of fibroblasts. No wandering or phagocytic cells made their appearance at any time, although the stained sections of the fixed gland were crowded with Gaucher cells.[9]

The fact that Gaucher cells could be demonstrated in stained sections of the lymph node and that they would not grow in vitro lends some support to the theory of pathogenesis held by Pick, i. e., that the failure of the typical large cell of Gaucher's disease to appear was due to lack of a stimulus to its formation. In vivo the stimulus (kerasin) may be the result of a primary disturbance of lipid metabolism. Further attempts, however, will be made to culture these cells, using, if possible, lymph nodes in which early involvement can be demonstrated.

The generalized convulsions which the boy suffered at the time the disease process was first noted probably were not related to Gaucher's disease. Neurologic symptoms, however, may occur with the chronic form of the disease; they are due to the invasion of nerve tissue by the Gaucher cells. With the acute type of the disease occurring in infants, nervous symptoms are a constant and prominent feature. Involvement of the nervous system with both acute and chronic forms usually is progressive. In the boy the convulsions disappeared spontaneously after a short period (three months) and left no residual signs.

Recently, the frequent occurrence of myopia, the presence of a malar flush and a characteristic symmetric pigmentation of the legs have been described in reports of Gaucher's disease.[2a] Because of the race of

9. Dr. Duncan C. Hetherington of the Department of Anatomy, Duke University School of Medicine, cultured the tissue. Tissue cultures of a lymph node were also made and studied by Mrs. M. R. Lewis and Drs. A. R. Rich and G. D. Gey of the Johns Hopkins School of Medicine, Baltimore, who presented the following report: "None of the characteristic (Gaucher) cells grew out, although they were present in sections of the node, and lymphocytes and connective tissue grew out excellently."

the children discussed here, pigmentation and malar flush would not be visible. Acuity of vision was not tested, but grossly it appeared to be normal.

The nonprotein nitrogen, calcium, phosphorus and serum protein contents of the blood at various periods were within normal limits. Both patients had creatinuria, but this often occurs in normal children. The basal metabolic rates were normal (table 2). Thyroid disturbances may occur late in the course of Gaucher's disease, but there was no evidence of thyroid dysfunction in these patients.

TABLE 2.—*Chemical Findings in the Blood and in the Urine and the Basal Metabolic Rates During the Various Hospital Admissions*

	Nonprotein Nitrogen, Mg. per 100 Cc. Blood Serum	Calcium, Mg. per 100 Cc. Blood Serum	Phosphorus, Mg. per 100 Cc. Blood Serum	Refractive Index	Total Protein, Gm. per 100 Cc. Blood Serum	Albumin, Gm. per 100 Cc. Blood Serum	Globulin, Gm. per 100 Cc. Blood Serum	Total Creatinine and Creatine, Mg. per 100 Cc. Urine	Creatinine, Mg. per 100 Cc. Urine	Creatine, Mg. per 100 Cc. Urine	Basal Metabolic Rate
Marshall L.											
7/7/36 to 8/19/36	30	..	...	1.3483	....	....	...	(Vol. 790 cc.) 55 0.43 Gm. per 24 hr.	33 0.26 Gm. per 24 hr.	22 0.17 Gm. per 24 hr.	.....
3/5/37 to 3/24/37	33	11	5.4	1.3491	6.65	3.75	2.9	..	..	..	Plus 11 per cent
5/17/37 to 5/22/37	31	..	...	1.3471	6.3	3.4	2.9	..	..	..	.....
Mary L.											
7/7/36 to 8/19/36	31	..	...	1.3496	....	....	...	(Vol. 745 cc.) 117 0.87 Gm. per 24 hr.	58 0.43 Gm. per 24 hr.	59 0.44 Gm. per 24 hr.	.....
3/5/37 to 3/24/37	24	9.4	5.4	1.3502	7.4	3.3	4.1	..	..	..	Plus 14 per cent
5/17/37 to 5/22/37	31	..	...	1.3471	6.3	3.4	2.9	..	..	..	.....

The lipid content of the blood of children has been shown to be considerably lower than that of adults.[10] Total lipid and phospholipid values in the cases presented here were within normal limits. However, total cholesterol and both its fractions (ester and free) were considerably below normal. Low cholesterol values frequently are found in the blood of patients with Gaucher's disease. The neutral fats, which are calculated by difference, are relatively high as a result of the diminution of the total cholesterol (table 3). Analysis of the percentage distribution of the lipids of the plasma as compared with that of normal children [10]

10. Erickson, B. N.; Williams, H. H.; Hummel, F. C., and Macy, I. G.: The Lipid and Mineral Distribution in the Serum of Normal Children, J. Biol. Chem. **118**:15, 1937.

shows similar values for free cholesterol and phospholipids but considerable difference in cholesterol esters and neutral fats (table 4).

The two children were given 500 cc. of milk containing 20 per cent cream (approximately 5 Gm. of fat per kilogram of body weight) after a fourteen hour period of starvation. A specimen of blood was taken during fasting, and determinations of the lipid content and iodine number were made two, four, six and eight hours after the test meal.[11]

TABLE 3.—*Blood Lipids in the Plasma* on July 13, 1936*

	Normal Adults†	Normal Children‡	Marshall	Mary
Total lipids	735 ± 216	336 - 606 (average 454)	412	332
Iodine number	.....	.....	95	111
Cholesterol total	232 ± 62	126 - 281	80, 81§	65, 51§
Free	82 ± 17	17 - 46	27	21
Ester	..... (average 254)	109 - 235 (average 182)	53	44
Phospholipid	181 ± 71	52 - 175 (average 126)	110	92
Neutral fat	225 ± 137	0 - 178 (average 100)	222	175

* Figures represent milligrams per hundred cubic centimeters of plasma. Total lipid fats and iodine numbers were obtained by the method described by W. R. Wilson and J. P. Hannen (J. Biol. Chem. **106**: 323, 1934). Total cholesterol was determined by the method of G. E. Sackett (J. Biol. Chem. **64**: 203, 1925). Cholesterol esters were determined after precipitation of the free cholesterol by digitonin. The free cholesterol was then determined by difference. Phospholipids were determined by the method described by C. H. Fiske and C. J. Subbarow (J. Biol. Chem. **66**: 375, 1925) on a Bloor alcohol-ether extract. Neutral fat was determined by difference.

† Page, I. H., and others: J. Biol. Chem. **111**: 613, 1935.

‡ Erickson, B. N., and others: J. Biol. Chem. **118**: 15, 1937.

§ March 16, 1937.

TABLE 4.—*Percentage Distribution of Lipids in the Plasma*

	Cholesterol Esters, Percentage of Total Lipid	Free Cholesterol, Percentage of Total Lipid	Free in Total Cholesterol, Percentage	Phospholipid, Percentage of Total Lipid	Neutral Fat, Percentage of Total Lipid
Normal children*	30-34	5-10	18-39	14-36	0-37
Marshall L.	13	7	34	27	54
Mary L.	13	6	32	28	53

* Erickson, B. N., and others: J. Biol. Chem. **118**: 15, 1937.

The curves for both children are similar; both showed a rise of total lipids after two hours, increases of 40 and 48 per cent after four hours and maximum rises of 53.3 and 53.7 per cent after six hours. The iodine numbers of the blood, however, showed a marked decrease (fig. 7).

A review of the reported changes in the blood lipids after the ingestion of fat shows considerable variation. The inconsistent findings are

11. Dr. H. M. Taylor of the Department of Biochemistry, Duke University School of Medicine, made the studies on fat.

probably due to (1) different technics in the determination of blood lipids, (2) variation in the type of fat used in the tests, (3) variation in the doses of fat given per kilogram of body weight, (4) a period of fasting not sufficient to establish a constant level of blood lipids and (5) uncontrollable factors which regulate the rate of absorption of fat from the intestine and its removal from the blood by the tissues.[12] Roney and Levy [13] fed a group of normal adults 500 cc. of milk containing 20 per cent cream and obtained a uniform curve of fatty acid

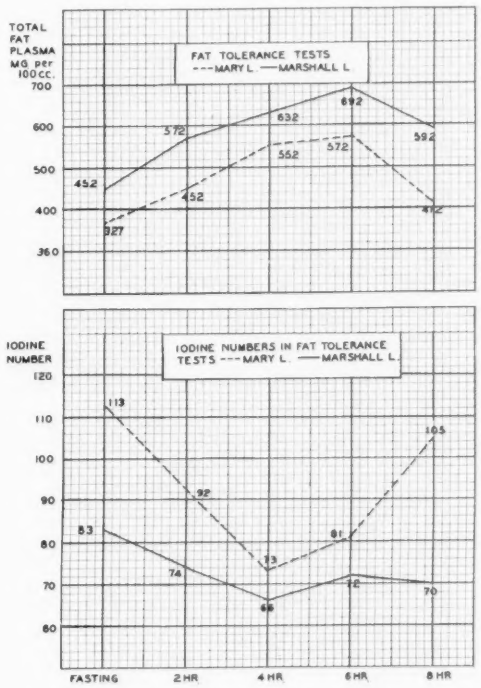

Fig. 7.—Curves of the blood lipids and iodine numbers after the ingestion of a substance (cream) high in saturated fatty acids (5 Gm. of fat per kilogram of body weight).

content in the blood. The maximum increase of 32 per cent occurred from three to five hours after the test meal. Blood cholesterol was also determined, but no change in this substance was found. Bloor [14]

12. Chaikoff, I. L.; McGavock, T. H., and Kaplan, A.: The Blood Lipids in the Post-Absorptive State and After the Ingestion of Fat in Normal Human Subjects and in a Case of Disseminated Cutaneous Xanthomata, J. Clin. Investigation **13**:1, 1934.

13. Roney, H. R., and Levy, A. J.: Studies on Fat Metabolism: Fat Tolerance in Obesity—A Preliminary Study, J. Lab. & Clin. Med. **15**:221, 1929.

14. Bloor, W. R., in Luck, J. M.: Annual Review of Biochemistry, Stanford University, Calif., Stanford University Press, 1933, vol. 2, p. 149.

reported that when a person is at rest, the ingestion of 1 Gm. of fat per kilogram of body weight is followed by a slow rise in the blood fat content, which reaches a maximum in four hours and returns to normal in six or seven hours. Man and Gildea [15] found that in normal adults a fat meal of 3.5 Gm. per kilogram of body weight produces a consistent rise of at least 34 per cent in the serum fatty acids; the rise usually begins in two hours, reaches a maximum in from three to five hours and returns to normal in seven or eight hours.

Wile, Eckstein and Curtis [16] studied the blood lipids of 3 adults with xanthomatous lesions of the skin. After the injection of 100 cc. of olive oil, the total lipid content of the blood in these patients remained unchanged for two hours and rose at the end of four hours to its maximum increase of from 19 to 27 per cent. The cholesterol content in all 3 cases remained stationary. Chaikoff, McGavock and Kaplan [12] found no difference in the response of the blood lipids to ingested olive oil (1.4 Gm. per kilogram of body weight) in a case of disseminated cutaneous xanthomata as compared with that of normal adults. They noted that the lipemic curve varied markedly with different persons; in some there was no rise, and in others an increase as high as 35 per cent occurred.

Cowie and Hoag [17] obtained the maximum rise of the blood lipids in from five to seven hours in children who had been fed cream after fourteen hours of starvation. Wilson and Hanner [18] studied the changes in the blood lipids and iodine number in children following the intake of milk containing 40 per cent cream and after ingestion of cod liver oil. Determinations were made at three different periods (during fasting and after two and four hours). An increase of the total lipids from 44 to 51.5 per cent was found at the end of four hours after both cream and cod liver oil. After the ingestion of cream (low iodine number from 30 to 40) the iodine number of the blood decreased, whereas after the ingestion of cod liver oil (high iodine number 155) an increase in the iodine number was obtained.

The percentage of increase at four hours and the maximum rise at six hours in our cases are in close agreement with the very few reported figures obtained for normal children. With the increase in the

15. Man, E. B., and Gildea, E. F.: The Effect of the Ingestion of a Large Amount of Fat and of a Balanced Meal on the Blood Lipids of Normal Man, J. Biol. Chem. **99**:61, 1932.

16. Wile, U. J.; Eckstein, H. C., and Curtis, A. C.: Lipid Studies in Xanthoma, Arch. Dermat. & Syph. **19**:35 (Jan.) 1929.

17. Cowie, D. M., and Hoag, L. A.: Studies in Blood Fat: A Preliminary Report, J. A. M. A. **77**:1493 (Nov. 5) 1921.

18. Wilson, W. R., and Hanner, J. P.: Changes of Total Lipid and Iodine Number of Blood Fat in Alimentary Lipemia, J. Biol. Chem. **106**:323, 1934.

total lipids was obtained the decrease in the iodine number which usually occurs after a test meal of saturated lipids.

The fat excretion in the stools is not believed to be a reliable indication of a disturbance in lipid metabolism.[19] Krakower [20] and Bauer [21] found very little relation between the intake and excretion of fat in normal adults and children. Hutchison,[22] however, reported that in normal infants and children, the percentage of fat in the feces varies from 20 to 46 per cent of the dry weight of the stool, providing the intake of fat is over 20 Gm. per day. The values obtained in our cases were within the normal limits in one case (Mary) and slightly below in the other [23] (table 5).

TABLE 5.—*Fat Excretion in the Stools with a Normal Fat Diet**

	Total Dry Matter, Gm.	Total Fat, Gm.	Fat Percentage
Marshall L.	10	1.69	16.9
Mary L.	20	4.54	22.7

* On July 24, 1936.

TABLE 6.—*Results of Tests for Function of the Liver*

	Van den Bergh Reaction, Mg. per 100 Cc.	Galactose Tolerance Test	Takata-Ara Test	Bromsulphalein Test	Phenolsulfonphthalein Test (Intravenous)
Marshall L.	Indirect 0.01	Negative	Negative	5 min., 10% retention 30 min., negative	Appearance at 5 min. 15% at 30 min. 40% at 60 min. 10% at 90 min. 5% at 120 min. Total 70% excretion
Mary L.	Indirect 0.01	Negative	Negative	5 min., 15% retention 30 min., negative	

The physiologic action of the liver can be measured to a limited extent by various tests. The results indicate that despite the tremendous enlargement of the liver there is no evidence of impaired hepatic function (table 6). Dextrose tolerance tests (1.75 Gm. per kilogram of body weight) showed a maximum rise in both cases after thirty minutes and return to the fasting level after three hours (fig. 8). The moder-

19. Fat in the Feces, Current Comment, J. A. M. A. **102**:935 (March 24) 1934. Hill, E., and Bloor, W. R.: Fat Excretion, J. Biol. Chem. **53**:171, 1922.

20. Krakower, A.: Fecal "Fat" and Its Relation to Fat in the Diet, Am. J. Physiol. **107**:49, 1934.

21. Bauer, E. L.: Celiac Disease, Am. J. Dis. Child. **35**:414 (March) 1928.

22. Hutchison, H. S.: Fat Metabolism in Health and Disease with Special Reference to Infancy and Childhood, Quart. J. Med. **13**:277, 1920.

23. Dr. R. Reiser of the Department of Medicine, Duke University School of Medicine, made the determinations of fat in the stools.

ately low amplitude of the curves might be due either to increased tolerance for sugar or to decreased absorption of this substance.

The esterification of cholesterol is believed to be a function of the liver. Normally from 50 to 75 per cent of the total cholesterol is present in the form of the ester. The values for cholesterol ester in the blood plasma have been found to parallel other indications of hepatic damage (jaundice, etc.), decreasing in advanced involvement and increasing with regeneration of the liver. The repeated determination of the cholesterol ester portion of the total cholesterol has been advocated as a means of diagnosing and following the course of parenchymatous disease of the liver.[24] Cholesterol esters in patients with these diseases were below the normal percentage of the total lipids, owing to the rela-

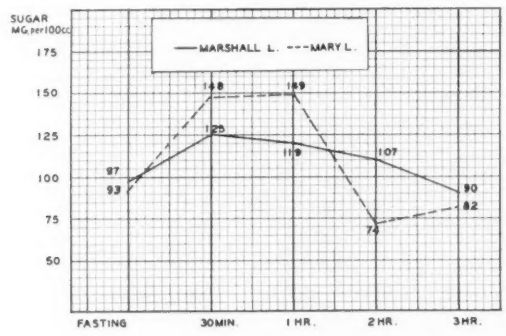

Fig. 8.—Dextrose tolerance, showing the moderately low amplitude of the curves (1.75 Gm. of dextrose per kilogram of body weight).

tively low total cholesterol values (table 3). However, the fractions of cholesterol esters in the total cholesterol are 65 and 66 per cent, within the values given for normal presons.

The rate of fat absorption and its possible value as an index of the function of the liver has also been studied. Sullivan and Fershtand[25] gave normal adults and a group suffering from various hepatic diseases a test meal of 120 cc. of cottonseed oil (from 1 to 1.8 Gm. per kilogram of body weight) and determined the total lipids of the plasma. In normal adults, the average postprandial rise at three hours was 30 per cent and at six hours 65 per cent, and at nine hours the lipid content had returned to the fasting level. In patients with diseases of the liver, the average rise at three hours was 8.9 per cent, at six hours 16.9 per cent and at nine hours 22.6 per cent. The conclusion was reached

24. Epstein, E. Z.: The Cholesterol Partition in Parenchymatous Diseases of the Liver, Arch. Int. Med. **47**:82 (Jan.) 1931.

25. Sullivan, M., and Fershtand, J. A. B.: Fat Absorption: Its Values as an Index of the Function of the Liver, Arch. Int. Med. **55**:834 (May) 1935.

that ". . . fat absorption curves of normal men and patients with diseases of the liver were sufficiently characteristic and different to be of aid in determining the status of the function of the liver." The fat absorption curves of the children with Gaucher's disease are similar to those of normal men.

Gaucher cells have been demonstrated in the kidney parenchyma.[26] Renal function has not been adequately tested in the reported cases. The nonprotein nitrogen determinations were consistently normal in these children. The phenolsulfonphthalein test (1 cc. given intravenously) in the boy resulted in normal appearance, time and rate of excretion (table 6).

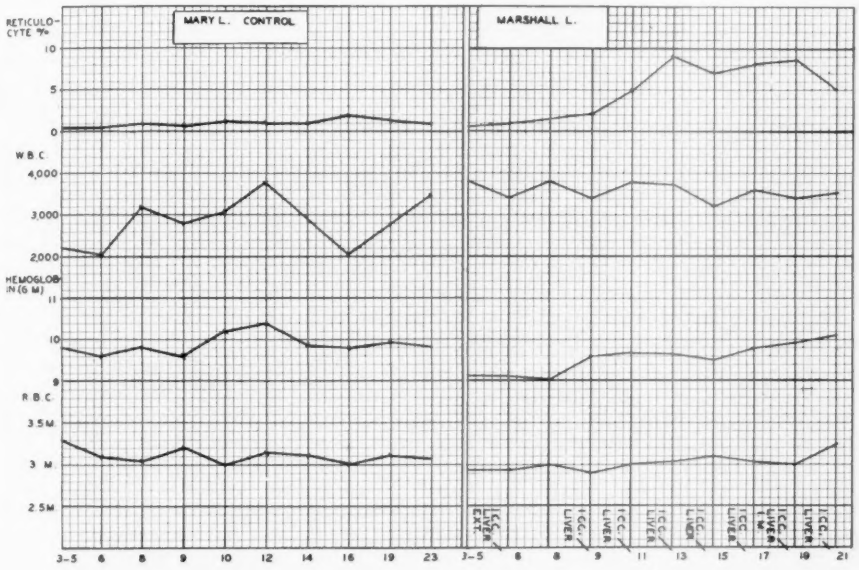

Fig. 9.—Response of the blood to intramuscular administration of liver extract. The figures at the bottom represent dates of medication (March 1937).

The treatment of chronic Gaucher's disease has been unsatisfactory. Splenectomy has been performed to remove the excessive weight of the organ, but the procedure is by no means curative. It results in a rather high mortality (20 per cent) and was not attempted for these patients. Roentgen therapy failed to have any effect on the size of Mary's spleen or liver. Potter and McCrae[27] reported a case of Gaucher's disease

26. Horsley, J. J., Jr.; Baker, J. P., and Apperly, F. L.: Gaucher's Disease of Late Onset with Kidney Involvement and Huge Spleen, Am. J. M. Sc. **190**:511, 1935.

27. Potter, E. B., and McCrae, C. C.: Gaucher's Disease, Am. J. M. Sc. **185**: 92, 1933.

in which noticeable reduction in the size of the spleen and marked general improvement followed parenteral administration of liver extract for nine months. Anderson,[2b] however, found that liver extract given his patient for eight weeks had no effect on the progress of the disease. Marshall was given 1 cc. of concentrated liver extract intramuscularly every other day for two weeks, and the response in the blood was studied. His sister was used as a control, and similar studies were done on the blood (fig. 9). There were a moderate reticulocyte response to the liver extract and a slight rise in the hemoglobin content and red blood cells. No change in the size of the spleen or liver was noted during this short period. The boy has been receiving liver extract [28] (1 cc. given parenterally every other day) since his last discharge, and his subsequent course is being followed. There appears to be no reason why liver extract should have any effect in cases of Gaucher's disease, but the inadequacy of other treatments warrants a clinical trial in these cases.

Best and Channon [29] demonstrated that the deposition of fat and cholesterol esters in the livers of depancreatized dogs can be inhibited by the addition of choline to the diet. Dragstedt and his associates,[30] however, have shown that the large amounts of choline necessary to obtain favorable results in depancreatized dogs are prohibitive. Dragstedt has succeeded in isolating a pancreatic factor (lipocaic) which given in relatively small amounts will prevent fatty infiltration of the liver in depancreatized animals to which insulin has been given. Although the cholesterol esters and lipids of the plasma of patients with Gaucher's disease are usually normal or below, determinations of the lipid and the cholesterol content of organs involved in the disease show much higher values for these substances (from two to two and a half times normal) than are found in normal tissues.[31] It is possible that the pancreatic substance might have a beneficial effect in this disease by preventing the deposition of fat in the body tissues.

Blood transfusions and preparations of iron may be given to combat the progressive anemia. Diets low in fat do not appear to have any effect on the course of the disease, which is chronic and usually ends in death from an intercurrent infection.

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28. The liver extract (1 cc. = 100 Gm. of liver) for use by the family physician at home was supplied by Lederle and Company. The potency has been tested and found adequate.

29. Best, C. H., and Channon, H. J.: The Action of Choline and Other Substances in the Prevention and Cure of Fatty Livers, Biochem. J. **29**:2651, 1935.

30. Dragstedt, L. R.; Van Prohaska, J., and Harms, H. P.: Observations on a Substance in Pancreas (a Fat Metabolizing Hormone) Which Permits Survival and Prevents Liver Changes in Depancreatized Dogs, Am. J. Physiol. **117**:175, 1936.

31. Horsley, Baker and Apperly.[26] Bloom, W., and Kern, R.: Spleens from Gaucher's Disease and Lipoid Histiocytosis, Arch. Int. Med. **39**:456 (March) 1927.

SUMMARY

Two cases of Gaucher's disease in Negroes are reported.

Changes in the blood, bones, bone marrow, spleen, liver, lymph nodes and conjunctivas have been demonstrated.

Tissue cultures of a peripheral lymph node were attempted, but Gaucher cells were not grown.

Normal blood lipid values were obtained, with the exception of those for total cholesterol and neutral fat.

The ingestion of milk containing 20 per cent cream was followed by normal fat tolerance curves in both cases.

The fat in the stools with a normal fat diet were within the limits given for normal children in one case and slightly below in the other.

The dextrose tolerance tests resulted in moderately flat curves. In both children, galactose tolerance, Takata-Ara and bromsulphalein tests gave normal responses. The phenolsulfonphthalein test in one case showed a normal rate of excretion.

Roentgen therapy had no effect in one case.

Liver extract administered parenterally in one case caused a reticulocytosis and a rise in the hemoglobin content and red blood cells. No change in the size of the spleen was noted.

NOTE.—The boy in case 1 received 1 cc. of liver extract regularly every other day for two weeks. From then on the injections were given irregularly, owing to lack of cooperation on the part of the parents. Treatment was discontinued entirely for two weeks, when epidemic parotitis developed. According to the last communication from the family physician (Aug. 10, 1937), the child was still active and appeared to be in fair health. There were no symptomatic complaints. The liver was as large as ever and had the same firm consistency.

MOTOR STABILITY IN CHILDREN WITH CEREBRAL PARALYSIS

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It is apparent to a casual observer that children with spastic paralysis are unusually reactive to any startling auditory stimulus. This study was undertaken in an attempt at a quantitative investigation of differences between normal children and children with spastic paralysis in motor stability and in the ability to adapt to a sudden auditory stimulus, with a view to correlating the findings with the symptoms and signs exhibited by the children with spastic paralysis.

SOURCE OF SUBJECTS

The paralytic children were tested at the Spalding School for crippled children through the permission of the board of education and the cooperation of Miss Thecla Doniat, principal. Only children with intelligence quotients above 50 were included in the study. The children came from the elementary grades and from some of the special divisions. There were no high school pupils. The ages ranged from 9 to 20, the majority of the children being in the middle teens.

A control group of normal children were tested at the Marks Nathan Jewish Orphans' Home through the courtesy of Mr. Ellis Trotsky. The normal children represented an age range essentially similar to that of the paralytic children. Of course the intellectual status and scholastic attainment of the control group were much higher than those of the paralytic group, many of the normal children being in high school.

The paralytic children were classified as hemiplegic, paraplegic or quadriplegic. Children with hemiparesis or with residuals of hemiplegia were, for purposes of this study, classified with the hemiplegic group. Similar practice was extended to the categories of paraplegia and quadriplegia. The children were also grouped according to the causes of the spastic paralysis, under the headings: trauma during birth, trauma after birth, encephalitis, hydrocephalus, tumor of the brain and unknown causes. Finally, the paralytic children were sorted out with reference to the accompanying symptoms of athetosis and convulsions. The normal children were classified as right handed and left handed.

THE EXPERIMENTAL PROCEDURE

Instruments.—The apparatus consisted of a metal plate with holes of graded sizes, a stylus, an electric counter and batteries. This apparatus was connected in

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a simple circuit, so that when the stylus touched the metal plate the circuit was closed and the electric counter registered. The child was instructed to keep the stylus in the center of the hole, it being explained to him that when the plate was touched a point was scored against him. The auditory stimulation was a loud buzz heard through the head phones and produced by completing a connection with a 60 cycle alternating current.

Procedure.—The experimental procedure was simple and was the same in each case. The child was first permitted to recline on a couch for five minutes in order to become acclimated, quieted and somewhat rested. He was then instructed as to his part in the experiment. He held the stylus successively in different holes for thirty seconds, beginning with a hole of 6 mm. in radius and proceeding with successively smaller holes. When he had completed the series of holes, the procedure was repeated with the head phones in place, and an auditory stimulus was sounded in the head phones every five to ten seconds, strict regularity being avoided because it was found less effective in disturbing the patient than were irregularly spaced stimuli.

Records such as tables 1 and 2 were obtained.

TABLE 1.—*Results of Test for Motor Steadiness in a Child with Spastic Paralysis*

Sex:	Female		
Age:	15		
Grade:	Special Division		I.Q. 51
Source:	Spalding School		
Illness:	Spastic paralysis; right hemiplegia		
History:	The birth was reported to be normal. The spasticity was apparent in infancy. When the patient was 5 weeks old she had "cramps," and "trembled all over." She had convulsions again at 5 months, when she had measles.		
	At examination there were observed a Babinski sign and an increased knee jerk on the right side. There were spasmodic contractions of the right arm, athetosis and disturbance of coordination.		
Comment:	The patient's whole body responded at first to the stimulus, and then the reaction resolved itself into a slight jerking of the paralyzed arm.		
Board 1	Trial I Right Hand		(Paralyzed)
Holes	1		
No stimulus	20		
Stimulus	34		
Diameter (mm.)	13		
Board 2	Left Hand		
Holes	1	2	
No stimulus	1	23	
Stimulus	35	53	Jerked the paralyzed arm
Diameter (mm.)	13	7	

Table 3 contains the average score in hole 1 (radius 6 mm.) for the right and left hands with and without stimulus. For some of the paralytic children the handicap was sufficiently severe to prevent one hand being used at all. The scores of such children were omitted in preparing the averages.

It is evident from the table that the score is related to the extent of the injury, the children with quadriplegia having a much larger number of errors than the children with hemiplegia. The children with athetosis had high scores. It is also apparent that the hemiplegic children did less well with the spastic hand.

TABLE 2.—*Results of Test for Motor Steadiness in a Normal Child*

Sex:	Female
Age:	12
Grade:	8B
Source:	Marks Nathan Jewish Orphans' Home
Illness:	None
History:	
Comment:	The patient was right handed. There was no body response to the stimulus.

Board 2	Trial I Right Hand					
Holes	1	2	3	4	5	6
No stimulus	0	0	2	6	8	17
Stimulus	0	0	2	5	8	11
Diameter (mm.)	13	7	6	5	4	3
Board 2	**Left Hand**					
Holes	1	2	3	4	5	6
No stimulus	0	0	0	2	8	11
Stimulus	0	0	0	2	8	8
Diameter (mm.)	13	7	6	5	4	3

TABLE 3.—*Average Score in Hole 1, Radius 6 Mm., Board 2.*

Paralytic Children

Condition	Number of Cases	Score: Right Hand, No Stimulus	Score: Right Hand, Stimulus	Score: Left Hand, No Stimulus	Score: Left Hand, Stimulus	Average Percentage of Increase of Errors with Stimulus: Right Hand	Average Percentage of Increase of Errors with Stimulus: Left Hand
Symptoms							
Left hemiplegia	13	8	14	11	23	75	109
Right hemiplegia	18	17	34	10	19	100	90
Paraplegia	8	10	23	8	15	130	87
Quadriplegia	11	26	45	30	55	73	83
Causes							
Trauma at birth	22	16	34	19	36	175	88
Trauma after birth	3	3	13	6	28	333	366
Encephalitis	12	10	20	8	17	100	112
Hydrocephalus	3	13	31	6	19	138	216
Tumor of brain	1	16	80	28	32	400	14
Unknown	9	15	25	15	23	66	53
Accompanying symptoms							
Convulsions	11	10	19	9	24	90	163
Athetosis	14	25	43	28	47	72	68
Total	51	14	29	15	27	107	80

Normal Children

Subjects	Number of Cases	Score: Right Hand, No Stimulus	Score: Right Hand, Stimulus	Score: Left Hand, No Stimulus	Score: Left Hand, Stimulus	Average Percentage of Increase of Errors with Stimulus: Right Hand	Average Percentage of Increase of Errors with Stimulus: Left Hand
Right handed	16	0	0	0.18	0.18	...	...
Left handed	2	0	0	0	0	...	...

TABLE 4.—*Average Score in Hole 4, Radius 2.25 Mm., Board 2.*

Normal Children

Subjects	Number of Cases	Score: Right Hand, No Stimulus	Score: Right Hand, Stimulus	Score: Left Hand, No Stimulus	Score: Left Hand, Stimulus	Average Percentage of Increase of Errors with Stimulus: Right Hand	Average Percentage of Increase of Errors with Stimulus: Left Hand
Right handed	16	5	4	10	7	—20	—30
Left handed	2	3	2	3	2	—33	—33

Table 4 contains the scores of normal children on hole 4 (radius 2.25 mm.). It is apparent that the normal children made better scores with the auditory stimulation than without it.

SUMMARY

The results, together with some incidental observations, may be summarized as follows:

1. All the paralytic children were less able to adjust themselves to a startling auditory stimulus than were the normal children. This was particularly demonstrated by the fact that with the normal children the number of errors decreased when the auditory stimulus was used, while with the paralytic children the number of errors showed a large increase under auditory stimulation.

2. The paralyzed extremities practically always reacted by movement to the auditory stimuli. In children with hemiplegia the affected hand was less steady both with and without stimulus, and those who were classified as quadriplegic reacted still more intensely. This seems logical, since presumably the extent of the injury to the brain is greater in the children afflicted with quadriplegia.

3. Great unsteadiness and severe reactions were observed in the children with athetosis.

4. A pronounced inferiority of immediate recall was evident in many of the paralytic children. They easily forgot from time to time which hole they had had the stylus in last.

CONCLUSIONS

1. Children with cerebral spastic paralysis are unable to adjust readily to a repeated auditory stimulus of an intensity which does not as a rule diminish the motor steadiness of the normal child.

2. The distribution and degree of motor unsteadiness and the reactivity of the skeletal muscles seem to depend largely on the distribution and degree of the spastic paralysis.

3. Children with athetosis react much more severely to a sudden auditory stimulus than do those with spastic paralysis only. This reactivity is absolutely excessive, but in view of the high initial unsteadiness it is not relatively excessive. The foregoing facts may be rationalized, according to our present understanding, as due to diminished cerebral inhibition of the reflex motor response to a sudden auditory stimulus in children with cerebral paralysis.

ACUTE PYURIA DUE TO DYSENTERY BACILLI

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The discovery within a period of a few months of 5 cases of acute pyuria in which dysentery bacilli were isolated from the urine aroused enough interest locally to prompt the present report. The occasional urinary complications of typhoid and paratyphoid fever and of bacillary dysentery are common enough to preclude the necessity for discussion of them; the occurrence of acute pyuria due to a dysentery bacillus without an antecedent history of dysentery is, as far as I have been able to learn, unreported in the literature.

Several of the statistical studies of the bacteriology of urinary infections have showed instances in which typhoid, paratyphoid and dysentery bacilli have been isolated from the urine,[1] but none of these reports has included sufficient clinical data for analysis, and it is probably justifiable to assume that these instances represented complications of frank intestinal infections. Several reports of isolated cases in which the condition was described as dysenteric pyuria warrant comment. In 1925 Calalb and Ionesco [2] reported an incompletely studied case of acute urinary infection due to a dysentery bacillus. The cursory history prevents analysis of this case. Cheatham, [3] in 1934, described as a complication of pregnancy a case of acute pyuria due to a dysentery bacillus (Flexner). Although the organism was not isolated from the stools, the patient had had diarrhea. In 1936 Pacheco and Magalhães Pecego [4] published the report of a 27 year old woman with a history of

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1. Kretschmer, H. L.: Diseases of the Urinary Tract in Infancy and Childhood, Surg., Gynec. & Obst. **53**:129 (Aug.) 1931. Gondolf, H. J., and Stringer, M. S.: The Bacteriologic Study of the Gram Negative Bacilli Found in Fifty Cases of Infection of the Urinary Tract, New Orleans M. & S. J. **81**:735 (April) 1929. MacKenzie, D. W., and Cochrane, W. J.: A Preliminary Report of the Bacteriology of Ureteral Cultures, Canad. M. A. J. **14**:293 (April) 1924. Young, H. H.; Colston, J. A. C., and Hill, J. H.: Infections in the Genito-Urinary Tract and Their Complications, J. A. M. A. **98**:715 (Feb. 27) 1932.

2. Calalb, G., and Ionesco, V.: Pyelonephritis Caused by Dysentery Bacilli, Compt. rend. Soc. de biol. **92**:1460 (May 29) 1925.

3. Cheatham, G. R.: Pyelonephritis of Pregnancy Due to a Dysentery Bacillus, Am. J. Obst. & Gynec. **28**:448 (Sept.) 1934.

4. Pacheco, G., and Magalhães Pecego, J. J.: A Case of Dysentery Pyuria, Brasil-med. **50**:111 (Feb. 8) 1936.

repeated attacks of dysentery and of five years of renal pain and hematuria who had dysenteric pyuria. The organism could not be identified completely but obviously belonged to the dysentery group.

A survey of the literature fails to reveal any other instances of acute pyuria due to dysentery; the following reports of 4 cases, then, represent the first cases of this type recorded.

REPORT OF CASES

CASE 1.—The patient, a 3 year old girl, had had frequent and fairly severe infections of the respiratory tract for two and one-half years. Nine days before her admission to the hospital fever, cough and coryza developed; four days later vomiting and nausea occurred. The stools were normal.

The family and past histories were noncontributory.

Examination showed a well developed, well nourished feverish child who did not look toxic. The detailed physical examination revealed no abnormality.

Laboratory Data.—The hemoglobin content was 85 per cent (Sahli). The count of red blood cells was 5,130,000 per cubic millimeter. The count of white blood cells was 15,400 per cubic millimeter, with 71 per cent of polymorphonuclear leukocytes. The Mantoux test (with 0.1 mg.) gave negative results. The urine was normal except for 4 or 5 white cells per high power field, but because of the unexplained fever cultures were made. On the day of entry a culture of the urine produced only Staphylococcus aureus; two days later gamma streptococci and Eberthella dysenteriae (Flexner) were isolated. Culture of the stool yielded no pathogenic organisms. One week after entry the patient's serum agglutinated E. dysenteriae (Flexner) in a dilution of 1:160.

Although the child did not look particularly toxic, the temperature rose to 104 F. on the second day and then by lysis fell to normal on the fifth day after admission to the hospital. There were never more than occasional white blood cells in the urine, and one week after entry the urine showed no dysentery organisms. No treatment directed at the urinary infection was given to the patient, and the recovery was obviously spontaneous.

CASE 2.—The patient, a previously well 5 year old girl, had a shaking chill, fever and general malaise three days before admission to the hospital. On the following day the temperature continued high, and a physician found pus in the urine. On the day before her admission to the hospital the temperature rose to 105 F. and she had a short generalized convulsion. There were no urinary symptoms. Slight constipation prevailed.

The family and past histories revealed nothing relevant to the present illness.

Examination showed an acutely ill, moderately toxic child who coughed frequently. The respirations were somewhat rapid but not labored. Moderate pharyngitis was present. The lungs were clear except for slight suppression of breath sounds at the base of the right lung. The heart, the abdomen and the reflexes were normal.

Laboratory Data.—The hemoglobin content and the red cell count were normal. The white cell count was 15,000 per cubic millimeter, with 75 per cent polymorphonuclear leukocytes. Two weeks later the white cell count had dropped to 4,500, with 45 per cent of neutrophils. The urine showed a moderate amount of albumin and many white cells singly and in clumps. On culture it yielded E. dysenteriae (Flexner). An examination of the stool one week after entry showed occasional pus cells, and E. dysenteriae (Flexner) was obtained on culture. Culture of the

blood was sterile. A roentgenogram of the chest showed minimal evidence of bronchopneumonia.

During the first week in the hospital the child had a septic temperature, with fluctuations from 99 to 105.6 F. The urine remained about the same, and obstinate constipation persisted. When after one week of forcing of fluids no improvement was seen by clinical or laboratory examination, treatment with ammonium mandelate (in the form of a syrup), 12 Gm. per day, was started. Within three days the temperature fell to normal, the p_H of the urine dropped below 5 and the amount of pus diminished noticeably. The appearance of vomiting necessitated the omission of therapy. At this time the parents requested that the patient be discharged, although culture of the urine was still yielding bacteria and white cells were reappearing in the urine in large numbers. Culture of the stool was sterile. After the child's discharge to her home the temperature rose to 103 F., with the recurrence of pyuria. After one week, treatment with methenamine and ammonium chloride was started. The temperature subsided rapidly, and the urine became completely clear in another week.

CASE 3.—The patient, a previously well 12 year old girl, showed fever, anorexia and pain on the right side of the abdomen three weeks before entry. These symptoms recurred at intervals of two to four days until the time of entry. Constipation prevailed throughout the illness.

Examination showed a rather obese, feverish girl who did not look toxic. Detailed examination showed an entirely normal condition except for slight pharyngeal injection and some tenderness in the lower part of the abdomen bilaterally.

Laboratory Data.—The hemoglobin content and the red cell count were normal. The white cell count was 16,700 per cubic millimeter, with 84 per cent polymorphonuclear leukocytes. The urine showed a small amount of albumin. There were many white cells, both singly and in clumps. Culture of the urine produced E. dysenteriae (Hiss-Russell). Repeated culture of the stool failed to yield pathogenic organisms. The patient's serum agglutinated stock E. dysenteriae (Hiss-Russell) in a dilution of 1 : 40.

During the first three days the temperature varied from 99 to 104 degrees F., and then dropped to normal. With no treatment (except for the forcing of fluids) the urine began to clear. On the fourth day ammonium mandelate (12 Gm., in a syrup) was started, and fluids were restricted to 1,000 cc. The p_H of the urine dropped rapidly to 4.8, and five days after treatment was started the urine had only an occasional white blood cell and was sterile on culture. The patient was discharged to her home, cured, eleven days after entry.

CASE 4.—The patient, a previously well 2½ year old girl, showed listlessness and gross pyuria three weeks prior to her admission to the hospital. This was followed by fever, frequent voiding of urine, nocturia and dysuria. No vomiting or diarrhea was noticed.

The family and past histories were irrelevant.

Examination showed a well developed, well nourished feverish girl who did not look toxic. Detailed examination revealed no abnormality except hypertrophy of the tonsils and adenoids, together with slight tenderness over the bladder.

Laboratory Data.—The hemoglobin content was 64 per cent (Sahli), the count of red blood cells was 3,970,000 per cubic millimeter and that of white cells was 21,000 per cubic millimeter, with 66 per cent of polymorphonuclear leukocytes. The urine showed albumin, acetone and many white cells singly and in clumps. Culture of the urine yielded E. dysenteriae (Flexner). Culture of the stool yielded no pathogenic organisms. The patient's serum failed to agglutinate stock strains

of E. dysenteriae (Flexner) when first tested (eleven days after entry) but did so in a dilution of 1:160 ten days later.

During the first six days the temperature ranged from 99 to 105 F. and, after remaining normal for a few days, again ran a high and irregular course for three days during the latter part of the second week. Treatment during this time consisted only in forcing fluids and giving alkali for relief of dysuria. Because there was still marked pyuria after the fever subsided, fluids were restricted (900 cc. per day) and ammonium mandelate (12 Gm., in a syrup) was given at the beginning of the third week. The p_H of the urine failed to fall below 5.6 until 15 grains (0.97 Gm.) of ammonium chloride three times a day was added to the treatment. There then followed a prompt fall in p_H to 5, the pyuria cleared rapidly and the urine became sterile. The child was discharged well three and one-half weeks after entry.

A fifth case in which dysentery bacilli were recovered from the urine of a child with an acute recurrence of a chronic urinary infection and no history of dysentery is not included because I was denied the opportunity of following her illness.

COMMENT

It must be assumed that the dysentery organisms reach the urinary tract by the same route followed by the colon bacilli in cases of ordinary pyelonephritis. From the standpoint of pathogenesis, urinary infections caused by typhoid bacilli are not analogous to those caused by dysentery bacilli, for, while in the former instance the frequent invasion of the blood stream [5] offers a route of infection, bacteremia in dysenteric infections is of great rarity.[6] In the small series of cases reported here, all the infections occurred in girls, and in none of them was there any reason to suspect septicemia. As in pyuria due to colon bacilli an ascending infection of the urinary tract is suggested by the sex incidence. In the few cases of dysenteric pyuria that have been reported in males [7] there have been a concomitant infection of the blood stream and diarrhea. The conditions described here in no way resemble such obviously overwhelming infections.

There was nothing characteristic about the clinical picture in the cases presented in this series. The symptoms were neither more nor less toxic than the symptoms of a similar infection due to colon bacilli might be. The temperature curve had no distinguishing characteristics. The spleen was not felt in any instance. In the absence of any history of gastrointestinal symptoms there was no clue to the nature of the infecting organism until its presence was revealed when culture of the urine was made.

The recovery without treatment observed in case 1, the improvement in case 3 prior to treatment and the fact that chronic dysenteric pyuria

5. Dietrich, H. F.: Typhoid Fever in Children, J. Pediat. **10**:191 (Feb.) 1937.
6. Rothman, P. E.: Dysentery Bacillemia, J. Pediat. **9**:167 (Aug.) 1936.
7. Brünauer, S. R.: Infections with Dysentery Bacilli, Wien. klin. Wchnschr. **29**:128, 1916.

has been reported only once [8] suggest that, like a comparable infection due to colon bacilli, pyuria due to dysentery bacilli is usually subject to spontaneous remission. Because, however, a single experimental observation had shown that mandelic acid is strongly bactericidal for E. dysenteriae (Sonne),[9] the trial of ammonium mandelate therapy seemed justified. In 2 cases, with the full dose for adults, which I have previously pointed out is necessary in the treatment of children,[9] the urine promptly became sterile. In the third case the occurrence of vomiting necessitated the omission of medication prematurely. Although the urine had cleared noticeably, the recurrence of frank pyuria and the persistence of bacilluria were observed after treatment with ammonium mandelate had been discontinued. After the child had a second bout of fever at home, the urine became sterile coincidentally with the administration of methenamine and ammonium chloride.

It is obvious that the diagnosis and treatment of dysenteric pyuria present no real difficulties. Interest in the condition is, however, twofold. From the standpoint of pathogenesis, the occurrence of the condition in patients who neither have nor have previously had clinical dysentery suggests that virulent dysentery bacilli may temporarily inhabit the gastrointestinal tract without causing clinical symptoms referable to that localization (case 3). Only when those particular organisms reach the genitourinary tract is an acute inflammatory process initiated. Finally, the importance and possible dangers of the condition from the standpoint of public health are obvious. Routine culture of the urine of all patients in hospital wards with acute pyuria will preclude the possibility of overlooking urinary infection due to dysentery bacilli.

SUMMARY

Four cases of acute pyuria due to dysentery bacilli are reported.

None of the patients had an antecedent history of dysentery.

The condition presents no distinguishing clinical features.

Recovery may be spontaneous.

Dysenteric bacilluria responds promptly to the administration of ammonium mandelate.

The disease may be of importance from the standpoint of public health.

NOTE.—Since this paper was submitted for publication, Neter [10] has reported 3 cases of a similar condition.

9615 Brighton Way.

8. Foerester, A.: A Case of Pyelocystitis Due to Dysentery Bacilli, München. med. Wchnschr. **65**:205, 1918.

9. Dietrich, H. F.: Sodium Mandelate as a Urinary Antiseptic in Children, Am. J. Dis. Child. **54**:496 (Sept.) 1937.

10. Neter, E.: Infections of the Urinary Tract Due to Bacterium Dysenteriae, J. Infect. Dis. **61**:338 (Nov.-Dec.) 1937.

CONVULSIONS COMPLICATING PERTUSSIS

A CLINICAL STUDY

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AND
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Convulsions in infants and children occurring during acute infectious diseases are sometimes minimized in their importance and seriousness by physicians. Many feel that a convulsion is either a manifestation of invasion by the infecting organism or the result of a high body temperature and is not in itself a serious clinical entity. However, this is not true of convulsions complicating pertussis, since the general mortality rate of 5 to 10 per cent for all hospitalized patients having pertussis uncomplicated by convulsions increases to 60 to 80 per cent when convulsions are present.

The purpose of this report is to point out the clinical features peculiar to convulsions occurring in 41 patients with pertussis, admitted to the Philadelphia Hospital for Contagious Diseases from 1933 to 1936, to attempt to determine the causes of their occurrence and to evaluate methods of combating them.

ETIOLOGY

In this series of cases the factors predisposing to convulsions included the following: (1) the age of the patient, (2) the severity of the paroxysms, (3) the presence of cyanosis, (4) the presence of bronchopneumonia and (5) congenital defects of the brain.

Chart 1 shows the age of the 41 patients. Chart 2 indicates the stage of pertussis at the time convulsions occurred. Of the 41 patients, 75 per cent were under the age of 1 year, and 82 per cent were in the first four weeks of the disease, the majority (53 per cent) showing the occurrence of convulsions from the second to the fourth week (whooping stage). In this group of 41 patients with convulsions, 12 had convulsions at the time of admission, and in 29 convulsions occurred during the period of hospitalization. Of the 29 patients in whom they first occurred after admission, 19 had definite and usually severe cyanosis before the seizure began. The cyanosis encountered was of two types: (1) a prolonged type which was usually present in patients in whom pertussis was accompanied by bronchopneumonia, and (2) an intermittent type, which followed frequent and severe paroxysms.

Twenty-eight patients had bronchopneumonia or otitis media, or both, before the onset of the convulsive state. Otitis media alone was

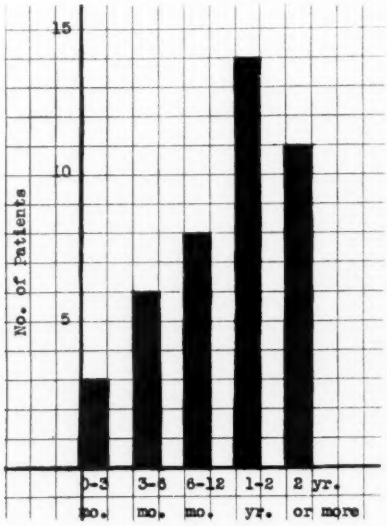

Chart 1.—Ages of patients with pertussis convulsions.

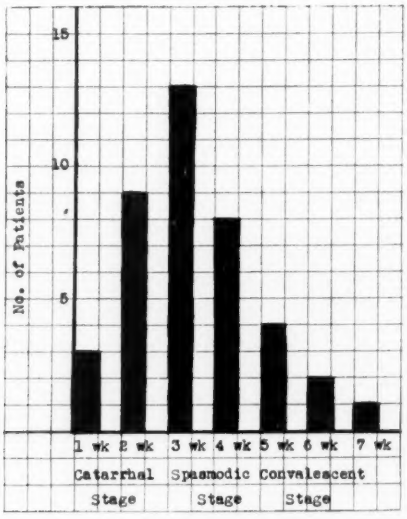

Chart 2.—Stage of pertussis at which convulsions occurred.

present in 5, bronchopneumonia alone in 14 and both in 9. The 18 patients without accompanying bronchopneumonia were chiefly those under 6 months of age, who suffered severe paroxysms of coughing with frequent prolonged periods of apnea and cyanosis.

In the presence of any of these predisposing factors, the actual exciting cause varied. Since in many cases convulsions first occurred while the patient was in the hospital, it was observed that a severe paroxysm of coughing usually preceded the onset of the convulsion, but occasionally convulsions occurred during some therapeutic procedure, such as a transfusion, a spinal tap, an aspiration of the throat or a feeding (often a nasal feeding).

CONVULSIVE STATE

The convulsive state in pertussis began with a period of somnolence, during which the child was irritable when disturbed. This period was often of twenty-four or forty-eight hours' duration. Three patients had the Cheyne-Stokes type of respiration during this period of lethargy. Often in the beginning there was not a generalized convulsion, but rather a slight, scarcely noticeable twitching. This might be confined to the face, usually to one side, but it often included the fingers or the wrist of the same side. Several patients at the onset showed a generalized rigidity, arching the back and hyperextending the neck into opisthotonos, with spasticity of all the extremities. Within a short time most of the children then showed clonic movements of the head, eyes, face, leg and arm. This condition was usually unilateral and often alternated from one side to the other. The head and eyes turned upward and outward toward the convulsed side, and frequently there was a lateral nystagmus, with the quicker component to the same side. Diaphragmatic spasms gave a gasping type of respiration, which resulted in cyanosis in all cases. The duration of the convulsions varied, some being continuous while others were intermittent. If they were continuous the patient rarely survived more than eight to twelve hours, and even when the seizures were intermittent either the outcome was fatal or the convulsions ceased within twenty-four to forty-eight hours. In all instances the convulsive movements stopped and were followed by a period of stupor, which often continued into death within a few hours.

Of special interest is the state of the cardiovascular system during and after the convulsive period. As the convulsions progressed, there was definite cyanosis. The pulse rate rapidly increased, until in many patients it could not be accurately counted at the wrist; the beat became weak and thready. The blood pressure dropped, the diastolic pressure being imperceptible at most examinations, and in many instances there was suffusion of the skin of the extremities. In several cases petechiae or ecchymotic areas on the hands or feet were present. Pallor was present together with the cyanosis. In general, the cardiovascular picture was that of shock.

The temperature varied, but in the majority of patients it showed elevation during the convulsive state and just before death, values of 107 and 108 F. being not uncommon.

NEUROLOGIC SIGNS

Definitely localizing neurologic signs were absent. In the acute convulsive stage, as has been noted, movements were present on one side and included all the muscles of that side at the same time. During this stage all deep reflexes were found to be increased, and not unusually a bilateral positive great toe reflex and fleeting ankle clonus could be elicited.

Only 3 of the 18 patients that recovered had any residual neurologic signs. One child had weakness of the right arm which completely disappeared within a week. A second patient, who had convulsions on the left side in the acute stage, with hyperactive reflexes and nystagmus to the left, showed erythema and sweating over the entire right side of the body, definitely demarcated in the midline. At that time the axillary temperature on the left was 102 F. and on the right 104 F. Within two weeks there was paresis on the left side with spasticity and increased reflexes. This patient was seen several months later and had made a complete recovery. The third child has but recently been discharged from the hospital. He had convulsions on the left side; the convulsions were followed by hemiballismus. The condition finally left a spastic hemiplegia, which was still present at the time of his discharge.

It is difficult to make examinations of the eyegrounds of infants, especially when convulsions are present. However, in a few infants so examined there was no evidence of edema or hemorrhage.

LABORATORY STUDIES

Spinal taps were performed on 22 patients. Pressures were measured with a mercury manometer in only 10 instances; 8 of the 10 pressure readings ranged between 10 and 20 mm. of mercury, 1 was under 10 mm. and 1 was above 30 mm. The number of white cells in the spinal fluid varied. Seventeen specimens showed fewer than 10 cells per cubic millimeter; 3 showed counts ranging between 10 and 50 cells; 2 showed counts ranging between 50 and 100 cells, and 1 showed a count of more than 100 cells. The differential counts in all instances showed a high percentage of lymphocytes. The test for albumin gave positive results in all specimens of spinal fluid examined, whereas the test for globulin gave positive results in 16 specimens and negative results in 5. The sugar content of the spinal fluid was high in the majority of the specimens examined. Only 2 specimens showed

less than 60 mg. per hundred cubic centimeters; in 6 the content varied between 60 and 80 mg. and in 8 was above 80 mg. The chloride content was within normal limits in all specimens. Smears and cultures for organisms were all sterile (chart 3).

Blood counts were made for 35 patients. The white blood cells showed the usual lymphocytosis characteristic of pertussis. The red blood cells numbered above 4,000,000 per cubic millimeter in 28 patients and below that figure in 6. It is interesting to note that in 11

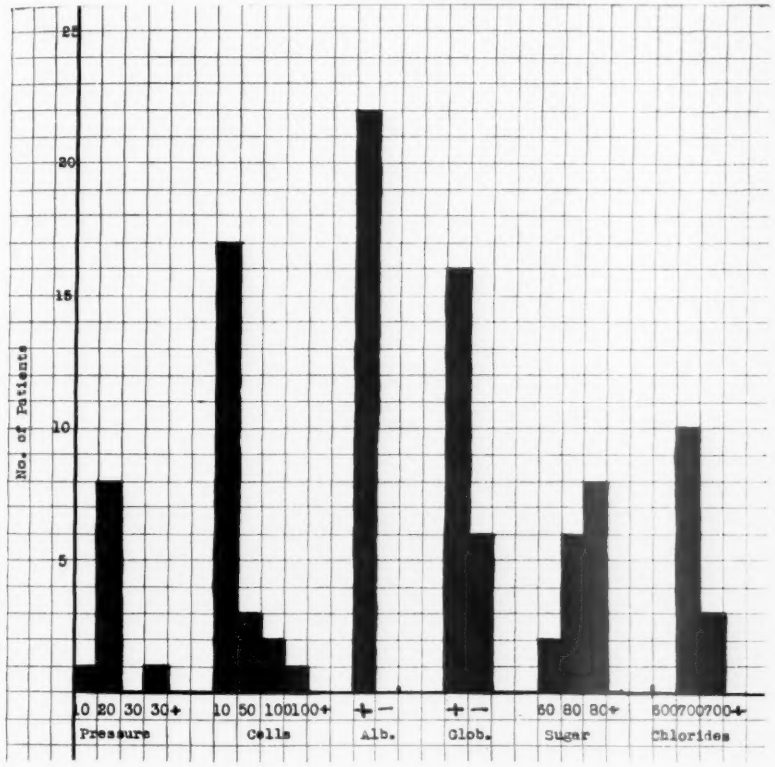

Chart 3.—Results of examination of spinal fluid.

patients changes were noted in the red blood cells, such as anisocytosis, poikilocytosis, polychromasia and stippling. The hemoglobin values did not correspond closely to the erythrocyte counts, the content of only 14 specimens being over 80 per cent; that of 17 specimens was between 60 and 80 per cent and that of 3 below 60 per cent.

Studies of the blood chemistry were not frequently made. The calcium content was normal in 3 instances, as was the carbon dioxide–combining power. Two determinations of total serum proteins showed normal values, but there was an increase in the albumin-globulin ratio.

MORTALITY RATE

The occurrence of convulsions during the course of pertussis greatly increases the mortality rate, which for all hospitalized patients varies from 5 to 10 per cent, to a rate of 78 per cent in the series here reported. H. Grenet and E. Mourrut [1] reported 24 cases, with a mortality of 87.5 per cent, and quoted Husler and Spatz's figure of 72 per cent and Ley and Degnelie's figure of 86 per cent. That the combination of convulsions and bronchopneumonia complicating pertussis makes the prognosis still more serious has been noted by the French investigators mentioned. In our series of 22 patients showing both convulsions and bronchopneumonia, the mortality rate was 66 per cent, as compared to 42 per cent for 19 patients having no bronchopneumonia.

THERAPY

Therapy in the presence of the convulsive state during pertussis is, as a rule, rather futile. The usual procedures are a spinal tap with or without complete drainage; hypnotics or sedatives, usually in the form of bromides and chloral hydrate given by rectum or morphine sulfate given by hypodermic injection. Ether in oil given by rectum has been used a great deal, as has also inhalation anesthesia with ether, ethyl chloride or chloroform.

Chloral hydrate and sodium bromide, as a hypnotic, was given to 30 children, usually in combination with some other therapeutic procedure. Ten of the 30 recovered. However, when the patients were classified as those who also received a transfusion and those who did not, we found 3 recoveries and 11 deaths in cases in which chloral hydrate and sodium bromide was not supplemented by a transfusion, but 7 recoveries and only 9 deaths when transfusions were added.

Spinal taps were done on the majority of the patients, with varying amounts of spinal drainage. This produced little apparent effect on the outcome.

The use of morphine sulfate and of inhalation anesthesia for overcoming the convulsive state should receive special attention only to be condemned. All 6 patients receiving such treatment reacted in the same manner; that is, convulsive movements were overcome for a short time by the anesthesia but returned, with cardiovascular collapse and death. Morphine sulfate failed to stop the convulsions in 4 patients; in fact, it made them worse. The other patients sank into stupor, with greatly increased temperature and pulse rate, cardiovascular collapse and death in a few hours. Chart 4 shows a typical example of this group.

1. Grenet, H., and Mourrut, E.: Les convulsions de la coqueluche, Bull. Soc. de pédiat. de Paris **31**:233 (May) 1933.

Calcium gluconate was administered in 10 cc. doses of a 10 per cent solution intramuscularly in 18 cases, with 8 recoveries. When calcium gluconate was used alone or with chloral hydrate and bromides there were 2 recoveries and 7 deaths, but when such therapy was combined with transfusions 6 patients survived and only 3 died.

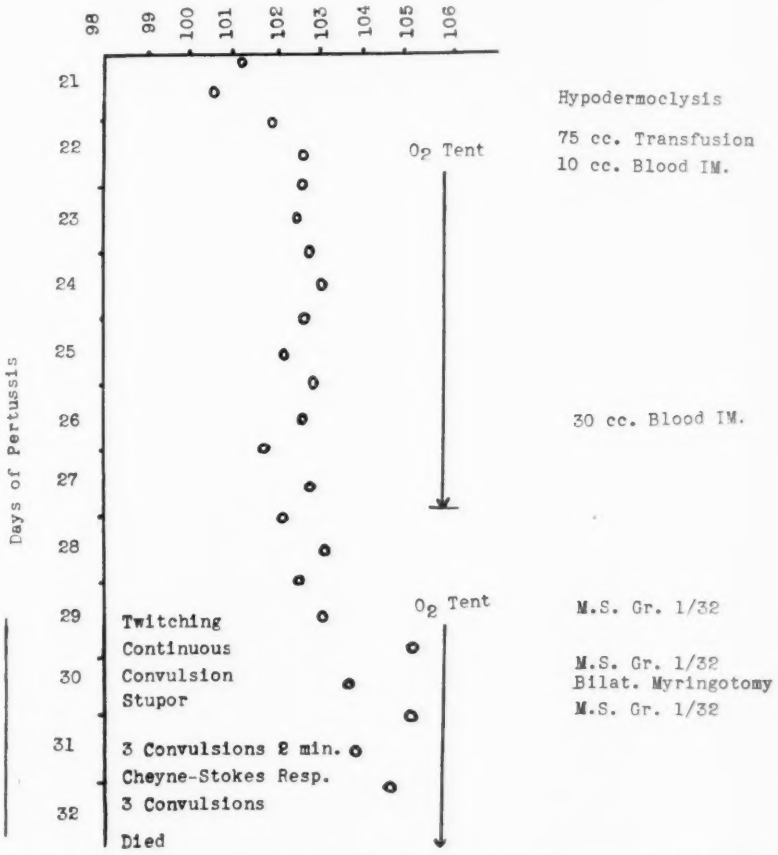

Chart 4.—Clinical record of A. K., aged 4 years, with pertussis, bronchopneumonia and later convulsions, receiving morphine sulfate.

Because of the cyanosis frequently preceding convulsions and always concomitant with them, oxygen was often used in treating convulsions. In the majority of cases it was given by nasal catheter after the convulsions began. Twenty-one children received oxygen; of these 7 recovered. When oxygen and transfusions were combined, 5 survived and 4 died.

In view of the terminal vasomotor collapse which followed the convulsions, it was thought that whole blood given intramuscularly might

have a vasotonic effect. However, of 4 patients thus treated, only 1 survived, and he had also received oxygen.

Best results were obtained when transfusions were used within twenty-four hours after onset of the convulsions. Eleven of 17 patients so treated recovered, making the mortality rate for this group only 35 per cent. It has been noted with all the therapeutic methods employed that when these were combined with transfusions the mortality rate was lowered. Chart 5 is that of a child recovering after transfusions and

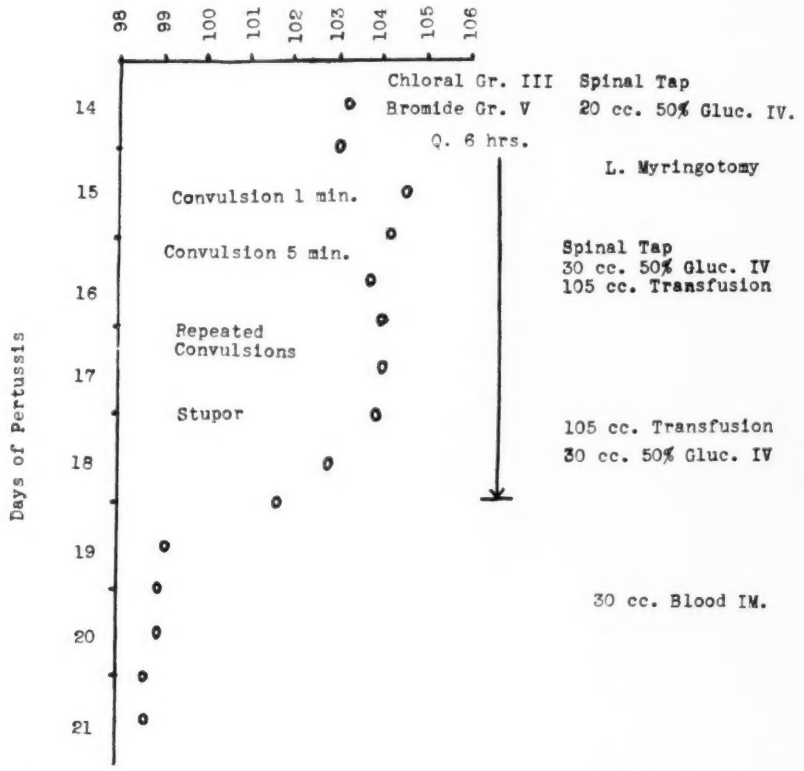

Chart 5.—Clinical record of W. M., aged 22 months, with pertussis, bronchopneumonia and convulsions, treated with transfusions.

is almost identical with the records of 8 of the 11 patients in this group who recovered. In the remaining 3 the recovery was more gradual, owing to the persistence of severe bronchopneumonia even after convulsive seizures had been arrested. That the patients in this group were not selected ones is apparent from the fact that it included 12 patients having associated bronchopneumonia; of these, 6 recovered.

Since pertussis vaccine has been in the foreground recently as a therapeutic as well as a prophylactic agent, 13 patients received this vaccine before the onset of convulsions; 6 of these patients died.

PATHOLOGIC PICTURE

The postmortem examinations were performed on 7 patients by Dr. Hershel C. Lennon. In none of these was there any macroscopic evidence of cerebral hemorrhage. The brains were all greatly edematous, several weighing one and a half times the normal weight for the patient's age. The sulci on the cortex tended to be obliterated by this edema. The veins on the surface of the cortex were distended, and the cortical tissue itself was pale and soft. In 2 brains evidence of small multiple petechial hemorrhages could be seen macroscopically as well as microscopically. There was but a slight increase in the amount of cerebrospinal fluid, and the ventricular system was not dilated.

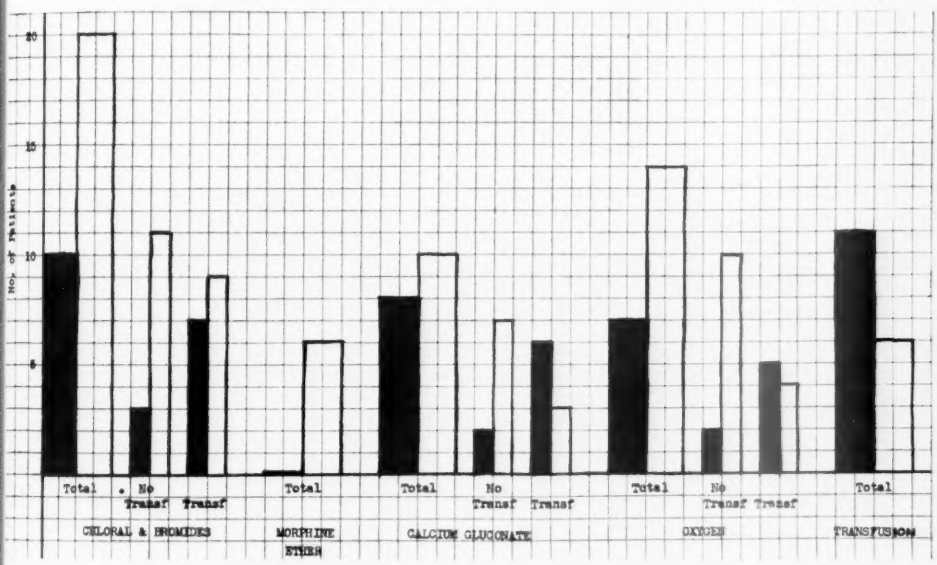

Chart 6.—Summary of therapy for pertussis convulsions. The solid black columns denote the number of recoveries; the columns outlined in black indicate the number of deaths.

The histologic picture in all our cases was chiefly that of cellular edema, with all the small venules distended as evidence of the congestion. As has been mentioned, 2 specimens showed evidence of multiple small hemorrhages in the cortex of the cerebrum and also in the cerebellum. One brain showed evidence of early perivascular lymphocytic infiltration, with slight endothelial proliferation and thickening in the small arterioles.

F. R. Ford [2] reported a case of pertussis and convulsions followed by diplegia in which there were complete degeneration and atrophy of

2. Ford, F. R.: Degeneration of Cerebral Cortex in Course of Pertussis, Am. J. Dis. Child. **37**:1046 (May) 1929.

the cortical cells. Likewise, F. Hiller and R. R. Grinker [3] observed softening of the gray matter in various stages in 1 case, and also ischemia, vascular congestion and endothelial proliferation of vessels in the areas showing this softening. In 15 autopsies, H. Grenet and E. Mourrut [1] found 3 brains with the typical picture of encephalitis, 2 normal brains and 10 brains showing only congestion and edema.

COMMENT

From the pathologic picture and clinical observations in this series of patients, it seems justifiable to make a statement as to the apparent causes of convulsions in pertussis. In the majority of patients, no specific pathologic change is present in the brain to point to an essential inflammatory cerebral disease as the etiologic agent; there are, rather, changes that may be attributed to an insufficient blood supply and to anoxemia. Clinically, convulsions usually occur in the spasmodic stage of the disease when the paroxysms are severe. This frequently results in venous congestion of the head and neck, with severe anoxemia, as is shown by the typical cyanosis developing during the paroxysm. In those patients having convulsions when pertussis is complicated by bronchopneumonia, cyanosis and inefficient circulation are instrumental in producing cerebral anemia and anoxemia. The facts that most of the convulsive movements involve many groups of muscles and that localizing neurologic signs are absent during and after the seizures also support the theory of a generalized chemical or mechanical change in the brain. Foster Kennedy [4] stated that the tonic stage is caused by congestion and edema. Likewise, Spiegel and Spiegel-Adolf [5] have shown experimentally that in the convulsive state there is a change in concentration on the surface of the nerve cells, with a decrease in density of the film on the cell surfaces, which causes increased permeability of the cells. They have produced these changes by inducing anoxemia, anemia, hydration and alkalosis. The immediate cause of death appears to be a generalized vasomotor collapse, probably due to the effect of the cerebral anoxemia on the vital centers.

That certain patients have definite encephalitis as the underlying cause is evident from the reports in the literature and from the fact that occasionally convulsions occur when paroxysms are mild and

3. Hiller, F., and Grinker, R. R.: Functional Circulatory Disturbances and Organic Obstruction of Cerebral Blood Vessels, with Contribution to Pathology of Pertussis Eclampsia, Arch. Neurol. & Psychiat. **23**:634 (April) 1930.

4. Kennedy, F.: Epilepsy and the Convulsive State, Baltimore, Williams & Wilkins Company, 1931.

5. Spiegel, E. A., and Spiegel-Adolf, M.: Physiochemical Mechanisms in Convulsive Reactivity, Proc. Soc. Exper. Biol. & Med. **34**:799 (June) 1936.

bronchopneumonia is absent. In fact, P. Fonteyne and J. Dagnelie,[6] by injecting endotoxin of Haemophilus pertussis intracerebrally and intrathecally, have produced in guinea pigs convulsions and histologic changes similar to those found in human patients.

With this knowledge of pertussis convulsions physicians can treat them more rationally. Since they are most likely to occur during the whooping stage and to follow a paroxysm, any therapeutic measure that will reduce paroxysms to a minimum may be definitely considered a prophylactic agent. The various vaccines given subcutaneously or intracutaneously are advocated by many clinicians, as are also ether in oil (given by rectum), barbiturates and opiates. However, in our experience convulsions have occurred even in patients receiving each of these remedies. We feel that cyanosis is a responsible causative factor; therefore, oxygen should be used early in all cases of bronchopneumonia and in infants having severe paroxysms even in the absence of bronchopneumonia.

Once convulsions have begun, the course of treatment, in the light of our experience, should begin with the use of barbiturates, given by mouth, by rectum or by the subcutaneous route. This should be supplemented with an immediate transfusion of whole blood and with the administration of oxygen (by means of a tent rather than by catheter). Tightly bandaging the extremities seems to help in a few cases.

Attempts to overcome cerebral anoxemia should also include treatment to decrease the cerebral edema. The limiting of the intake of fluids, repeated spinal drainage and intravenous injection of hypertonic solution of dextrose in many of our patients had no definite effect on the outcome. However, the future trial of sucrose solution injected intravenously or of concentrated lyophilic normal human serum seems indicated. The latter, theoretically, should prove of special value, because it would dehydrate the cerebral tissue as well as increase the blood pressure and help to overcome vasomotor collapse.

SUMMARY

Convulsions occurred as a complication in 41, or 8 per cent, of 516 patients with pertussis admitted to the Philadelphia Hospital for Contagious Diseases from 1933 to 1936 inclusive.

They were most frequent in children under the age of 2 years and during the spasmodic stage of pertussis.

Bronchopneumonia with severe cyanosis predisposes to their development.

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6. Fonteyne, P., and Dagnelie, J.: L'action de l'endotoxine coquelucheuse sur les centres nerveux, Compt. rend. Soc. de biol. **110**:978 (July 25) 1932.

Severe paroxysms are the chief inciting cause.

Neurologic localizing signs are usually transient and indefinite.

The spinal fluid is normal in the majority of patients. A slightly increased cell count (lymphocytes), positive reactions to tests for albumin and globulin and increased sugar content are the most consistent changes.

Convulsions in this series were usually followed by vasomotor collapse.

The mortality rate for the series was 78 per cent, but for 17 patients to whom transfusions were given the death rate was 35 per cent.

Cerebral congestion and edema were the most frequent pathologic changes.

EFFECT OF A MILK SUPPLEMENT ON THE PHYSICAL STATUS OF INSTITUTIONAL CHILDREN

I. GROWTH IN HEIGHT AND IN WEIGHT

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BLANCHE LENNING, S.M.

AND

MARGUERITE SCOTT, S.M.

CHICAGO

The ultimate test of what constitutes an optimum diet must be made on human beings under normal conditions of living. The usual method of attack on the problem is through carefully controlled laboratory experiments, in which the amount of one or more of the various dietary essentials needed to produce optimal storage is determined. Such studies are, indeed, essential to a fundamental understanding of nutritional needs. They are, however, costly and laborious, and so far as the period of childhood beyond infancy is concerned, only a bare beginning has been made by this means toward determining acceptable standards for the various dietary requirements. Even when such standards are eventually determined, they must still be tested in practical situations in terms of everyday foods before they will be generally accepted. One method of approach is to determine through large scale feeding the effect of adding certain basic foods to the diet on growth and physical status of children. Such experiments do not supplant the laboratory studies but rather support and supplement them. They afford, moreover, the type of evidence that will be accepted by the lay public as indicating that it does in reality make a difference whether a child receives a fully adequate diet or one giving only bare maintenance.

A number of such studies have already been reported. In most of these, growth has been used as the criterion for measuring the effect of the dietary supplement. One of the first and best controlled experiments of this type is that of Corry Mann [1] in England, who tested the

From the Department of Home Economics, University of Chicago.

1. Mann, H. C.: Diet for Boys During the School Age, Medical Research Council, Special Report Series, no. 105, London, His Majesty's Stationery Office, 1926.

effect over a two year period of a number of dietary supplements (milk, butter, margarine, casein, sugar, watercress) on growth in an institution housing about 350 boys on the cottage system. It was found that every supplement used caused improvement in growth over that of the controls. The greatest improvement resulted from the addition of a pint (473 cc.) of milk; the increase amounted to 2.13 pounds (966 Gm.) and 0.79 inch (2 cm.) in a year. It was concluded that the institutional diet was low in almost every dietary essential and that milk produced the greatest improvement because it supplied the largest number of these essentials. Dunstan [2] has recently subjected Mann's findings to further analysis. He noted that the boys in the group given milk were shorter and lighter at the beginning than the controls and concluded that this may have favored their spectacular gains. He stressed individual differences in growth and noted also that only in the groups given watercress and butter were there no subjects who failed to respond to special feeding. He stated the belief that this suggests a vitamin A deficiency.

To determine whether Mann's results could be duplicated in a school, Orr [3] and Leighton and Clark [4] carried out a similar study involving nearly 1,200 school children in Belfast and in seven cities and towns in England and Scotland. The supplements used were milk, skim milk and biscuit; they were given at school as a midmeal feeding. During the first year, both groups given milk averaged greater gains in both height and weight than did the group given biscuit (the control children). The following year the groups were reversed, the children who had had biscuit now receiving the milk, and those who had had milk now receiving biscuit. The results were likewise reversed, the children who received milk again making the best gains.

Sutherland [5] in Scotland studied the effect of added vitamins A and D on the growth of children and on their resistance to infection. The experimental group made an average increase in height of 2.3 per cent and in weight of 5.3 per cent over their original measurements; the controls made increases of 2.1 per cent in height and 4.9 per cent in weight. The difference in height in favor of the treated group was significant; that for weight was not. A survey of the diets of 66 families living in Peterhead showed that all were low in most of the dietary constituents. The author stated the belief that the difference

2. Dunstan, W. R.: Feeding Experiments, M. Officer **55**:227, 1936.

3. Orr, J. B.: Milk Consumption and the Growth of School Children, Lancet **1**:202, 1928.

4. Leighton, G., and Clark, M. L.: Milk Consumption and the Growth of School Children, Lancet **1**:40, 1929.

5. Sutherland, R.: Vitamins A and D: Their Relation to Growth and Resistance to Disease, Brit. M. J. **1**:791, 1934.

between his results and those of Mann and Orr is explained by the fact that the pint of milk in the latter instance made good more of the deficiencies than did his vitamin A and D supplements for the children in Peterhead.

In this country, Daniels [6] was among the first to demonstrate that superior growth may result from an improved diet. Two groups of infants were fed a diet of modified cow's milk; one group also had cod liver oil, the other did not. Retention of calcium, phosphorus and nitrogen was higher in the group receiving cod liver oil, their growth was superior and their output of urinary creatinine was also increased; this indicated that there was likewise a better development of muscle. Daniels concluded that the standards of growth formerly accepted are too low.

The largest series of studies of this type in this country was reported by Morgan and her co-workers.[7] They tested the effect of a number of dietary supplements (orange, milk, fig, wheat germ) on the growth of school children in California. In some groups milk produced the best gains; in others, orange. In one study wheat germ caused a marked improvement in growth, even in three months. The results appeared to depend on the dietary essentials which were most deficient in the locality.

Ross and Summerfeldt [8] demonstrated the value of an increased supply of vitamin B_1 and iron in the diet of children in a large orphanage. The control group was kept on the institutional diet; one group was given a concentrate of vitamin B_1, and the third had a special cereal containing additional vitamin B_1 and special minerals. The average gain was 3.6 pounds (1.6 Kg.) for the control children, 5.5 pounds (2.4 Kg.) for those given the concentrate and 7.5 pounds (3.4 Kg.) for those given the special cereal. The hemoglobin of the last group also showed an increase greater than that of the other groups. The effect

6. Daniels, A.; Hutton, M. K.; Stearns, G., and Hejinian, L. M.: The Relation of Rate of Growth in Infants to Diet, Am. J. Dis. Child. **37**:1177 (June) 1929.

7. Chaney, M. S.: A Comparison of the Value of Milk and Oranges as Supplementary Lunch for Underweight Children, Am. J. Dis. Child. **26**:337 (Oct.) 1923. Morgan, A. F., and Hatfield, G. D.: The Effect of Various Supplementary Lunches on the Plasma Carbon Dioxide Capacity of Children, ibid. **32**:655 (Nov.) 1926. Morgan, A. F.; Hatfield, G. D., and Tanner, M. A.: A Comparison of the Effects of Supplementary Feeding of Fruits and Milk on the Growth of Children, ibid. **32**:839 (Dec.) 1926. Morgan, A. F., and Tanner, M. A.: Supplementary Feeding of School Children, ibid. **33**:404 (March) 1927. Morgan, A. F., and Warren, L.: Stimulation of Growth of School Children by Small Supplementary Feedings, ibid. **36**:976 (Nov.) 1928. Morgan, A. F., and Barry, M. M.: Increased Growth Secured Through the Use of Wheat Germ, ibid. **39**:935 (May) 1930.

8. Ross, J. R., and Summerfeldt, P.: Value of Increased Supply of Vitamin B_1 and Iron in the Diet of Children, Am. J. Dis. Child. **49**:1185 (May) 1935.

of the same special cereal on the growth of 136 children up to 3 years of age in an orphanage was tested by Blatt and Schapiro.[9] The experimental children exceeded the controls in weight, length, stem length and circumference of chest and head. They also had earlier eruption of the teeth and an advantage in hemoglobin values.

The effects of giving a midmorning lunch of milk or tomato or a mixture of the two were studied by Wait, Merriam and Cowing [10] with 760 children in four rural schools in Massachusetts. A definite though not marked improvement was noted in the children who had the lunches, as evidenced by medical records, by gains in weight and by the general nutritional condition. No significant evidence of increased growth in height or in the arrest of dental caries was observed. The authors expressed the belief that the findings indicated limitations in the dietaries in the homes of these communities. These deficiencies seemed to be more effectively corrected by milk than by tomato, though either or both resulted in some improvement.

In a two year experiment in a day nursery, Rose and Borgeson [11] determined the effect of adding an egg a day to the diets of preschool children, using a variety of methods for assessing physical status. In most measurements no significant improvement could be noted for the experimental over the control group. The chief positive findings were a tendency for hemoglobin values to be consistently higher and for duration of colds to be shorter in the experimental group than in the group not given egg. It was noted that the diets of these children, even without the supplement, were better than average, and since the supplement was small in proportion to the total diet and since other variables undoubtedly entered in, it is not surprising that significant differences could not be demonstrated. Other studies showing the effects of improved diet on the arrest of dental caries and on other aspects of development will be reviewed in later articles dealing with these topics.

The significance of such studies as those just cited was recently pointed out by Orr.[12] He presented the challenging theory that the dietary standards attained by those whose incomes allow them free choice of food should be the standards for all classes of people. He stated the belief, moreover, that optimum nutrition should be regarded as that state of nutrition which is not susceptible of improvement by

9. Blatt, N. L., and Schapiro, E.: Influence of a Special Cereal Mixture on Infant Development, Am. J. Dis. Child. **50**:324 (Aug.) 1935.

10. Wait, B.; Merriam, O., and Cowing, M. V.: Supplementary Mid-Morning Feeding of Rural School Children, Bulletin 310, Massachusetts Agriculture Experiment Station, 1934, p. 47.

11. Rose, M. S., and Borgeson, G. M.: Child Nutrition on a Low-Priced Diet, New York, Columbia University Press, 1935, p. 109.

12. Orr, J. B.: Food, Health and Income, London, The Macmillan Company, 1936, p. 72.

the addition of any dietary supplement. The basis for this theory is that growth and development follow a hereditary pattern and that while it is possible for a child to fall short of his normal growth pattern, he cannot exceed it. When improvement in any aspect of development can be definitely demonstrated through a dietary supplement, it implies that the previous diet has been inadequate in one or more dietary constituents. If this point of view is accepted, this type of study should constitute an excellent supplementary method of determining under practical conditions what constitutes an optimum diet, as well as a means of demonstrating graphically that food does in reality make a difference, in terms that the average layman can understand.

PURPOSE AND GENERAL PLAN OF STUDY

The study reported here was undertaken in an attempt to determine (1) whether the daily addition of a pint of milk to the diets of children already receiving approximately 1 pint would produce any measurable improvement in physical status in a year and (2) whether any advantage could be demonstrated for irradiated over nonirradiated milk. The study was carried out from November 1934 to November 1935 in an institution housing approximately 150 children, the majority of whom were of grade school age. A large proportion of the children were of Scandinavian background; this made a more homogeneous group than is commonly found.

The children were divided into three groups, matched as closely as possible on the basis of age, sex, deviation from average weight for height and age, and condition of teeth. Accurate matching was of course impossible in so small a group, but by giving the odds first to one group then to another, three groups were formed which were reasonably comparable on the bases chosen. One group was left on the institutional diet as the control, one was given an additional pint equivalent daily of nonirradiated evaporated milk, and one, the same quantity of irradiated evaporated milk.

A battery of measurements were used to assess the children's physical status at the beginning of the experiment and their progress during the year. These included: (1) monthly measurements of height and weight, (2) Franzen indices of nutrition, (3) the Lucas-Pryor-Stolz width-length index, (4) roentgenograms of the wrists as a measure of bone development, (5) dental examinations for determination of the arrest or progress of dental caries and (6) medical examinations; the last 5 measures were applied at the beginning and end of the year. Although not related to the supplement used, capillary resistance was determined for all children five times during the year for the possible light the tests might throw on the adequacy of vitamin C in the dietary. Furthermore, in order to obtain some quantitative measure of the diet which was being supplemented, a serial dietary study was carried out during the greater part of the year. This consisted of a quantitative study of the diet for 1 child each week. The subjects were chosen successively from the various age levels and by trios from the matched groups. That is, if the first subject was a 3 year old control, he was followed by his mate in the group receiving plain milk and then by the mate in the group receiving irradiated milk. A 10 year old trio would then be similarly studied.

Since one third of the children were to receive no additional milk, the superintendent of the institution was unwilling to have it given as part of the regular meals. It was necessary, therefore, to administer it otherwise. To the nursery

children it was given at 10 in the morning; to the school children it was given at school as part of the noon lunch, and during week ends and vacations as a mid-morning or midafternoon supplement. Feeding at school was facilitated by the fact that the grade school children carried their lunches; it was a simple matter to have the experimental children eat in a room set apart for this purpose. Since their usual lunch consisted of four slices of bread spread with jelly or occasionally with butter or peanut butter, it seemed desirable to serve the milk warm, and cocoa proved to be the most acceptable form. Large glasses were used, and the entire pint of reconstituted evaporated milk, prepared as cocoa, was thus given in one serving.

In an experiment of this type it is essential that close and constant supervision be maintained in order to insure actual administration of the supplement and adequate checking of other details. Consequently a full time worker lived at the children's residence and was responsible for all details at that end. She prepared and administered the cocoa both at school and in the residence. She kept records of consumption of milk, of colds and other illnesses, of absence from the institution and of other factors which might influence the results. She carried out the dietary studies, made arrangements for all details of the numerous examinations that the study involved and assisted in these by keeping the children coming in proper order for the various tests.

The present report deals with the study on growth; other data will be reported in succeeding papers.

METHODS OF SECURING RECORDS OF GROWTH

Every effort was made to secure the most accurate measurements possible of growth in weight and height. Weights were taken on a Fairbanks platform scale and were recorded to the nearest 20 Gm. They were taken at the same time of day by the same two observers (one to take, the other to check and record); the subject wore only shorts of known weight, so that nude weight might be recorded, and was weighed after he had been to the toilet. Heights were taken by the same observer on a stadiometer under conditions which had previously been shown to secure the most reliable measurements.[13] Each child was given the following directions: "Heels together; head back and heels against the rod; head up, eyes looking straight ahead; stand as tall as you can without lifting your heels." Repeated tests on the same child showed that measurements taken by this procedure could be reproduced by a given observer within about 2 mm.

These measurements were taken at the beginning of the study in October, and at four week intervals thereafter for a full calendar year. As an aftercheck they were taken six months after the supplementary feeding had ceased. The records obtained by these means were subjected to a number of comparisons to determine whether a demonstrable difference existed between the growth of the group given the supplement and that of the group not given a supplement. These include: (1) mean gains in height and weight, (2) the percentage of the expected gain made by each group as a whole, (3) the percentage of children in each group who made the expected gains and (4) the relative gains of individual children in the matched trios. For only 107 of the 150 children were continuous records secured throughout the year; the data of these children are analyzed here. Of the 107 children, 36 were controls, 35 received plain milk and 36 were given irradiated milk. For brevity these groups will be designated hereafter as control, milk, and D milk groups.

13. Roberts, L. J.: Nutrition Work with Children, ed. 2, Chicago, University of Chicago Press, 1935, pp. 376-386.

MEAN GAINS OF THE THREE GROUPS

The total and mean gains in height and weight of the 3 groups are recorded in table 1 and chart 1.

It will be observed that the mean gains in both height and weight are somewhat greater for both the milk groups than for the control, with little difference between the groups given the two types of milk. The superiority of the groups given the supplement over the control

TABLE 1.—*Total and Mean Gains for the Year for the Three Dietary Groups*

Group	No. of Children	Height Gain in Cm.			Weight Gain in Kg.		
		Total	Mean	Probable Error of Mean	Total	Mean	Probable Error of Mean
Control	36	190.3	5.3	0.157	119.8	3.33	0.264
Milk	36	222.5	6.2	0.180	156.8	4.36	0.345
D milk	35	215.4	6.2	0.216	138.1	3.95	0.334

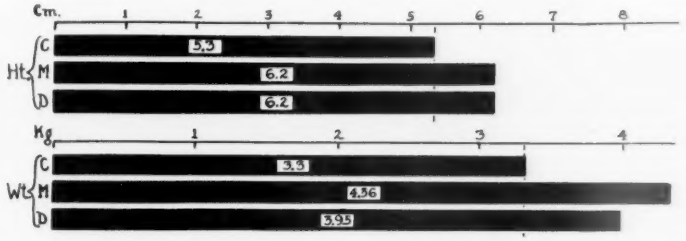

Chart 1.—Mean annual gain in height and weight for control group and for groups receiving plain milk (*M*) and irradiated milk (*D*) (table 1).

TABLE 2.—*Significance of Differences Between Mean Gains in Height and Weight for the Three Dietary Groups*

Groups Compared	Difference of Means	Probable Error of Difference of Means	Ratio of Probable Error to Difference
Height			
Milk over control	0.9	0.239	3.8
D milk over control	0.9	0.267	3.3
Milk over D milk	0.0	.....	...
Weight			
Milk over control	1.03	0.434	2.4
D milk over control	0.62	0.426	1.5
Milk over D milk	0.41	0.480	0.9

group amounts to 0.9 cm. (0.3 inch) in height for both types of milk, and in weight to 1.03 Kg. (2.27 pounds), and 0.62 Kg. (1.4 pounds) for the milk and the D milk group, respectively. These differences are not large, but they are consistently in the same direction. Moreover, statistical treatment of the data recorded in table 2 shows that the differences in height for the milk and the D milk group over the

control group are respectively 3.8 and 3.3 times their probable errors and are therefore probably significant. For weight the corresponding ratios of the differences of the two milk groups over the control group to their probable errors are 2.4 for the plain milk and 1.8 for the irradiated milk group. Although these differences, as judged by the

TABLE 3.—*Percentage of Expected Annual Gains in Height and Weight Made by the Three Dietary Groups*

Group	Total	Height			Weight		
		Average Gain, Cm.	Average Expected Gain, Cm.	Actual Gain as Percentage of Expected Gain	Average Gain, Kg.	Average Expected Gain, Kg.	Actual Gain as Percentage of Expected Gain
Control	36	5.3	5.0	106	3.33	3.06	109
Milk	36	6.2	5.3	117	4.36	3.59	122
D milk	35	6.2	5.4	115	3.95	3.34	118

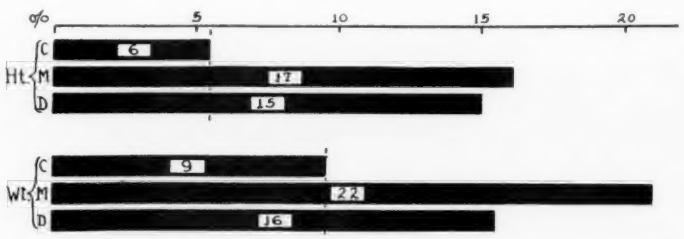

Chart 2.—Percentage in excess of annual expected gains in height and weight made by control group (*C*) and by groups receiving plain milk (*M*) and irradiated milk (*D*) (table 3).

ratios, do not attain significance, they are consistent and in the same direction as for height, and they probably represent real differences. There is no difference in height between the two milk groups, and the difference in weight is but 0.9 times its probable error. It would appear from this analysis that both the milk supplements produced small but probably significant increases in growth during a year's time, with little difference in favor of either the irradiated or the nonirradiated milk.

The superiority of the gains of the milk groups is even more evident when the actual gains are compared with the expected gains for the period. By means of the Baldwin-Wood tables, which give expected annual gain for each age by sex and type of build, the expected gain for each child in the study was determined, the results were totaled for each group, and the actual gains were expressed in percentage of the expected gain. The results are shown in table 3 and chart 2. While the control group made but 106 per cent of its expected gain in height,

the milk and the D milk group made 117 and 115 per cent, respectively. For weight the gains were 109, 122, and 118 per cent of the expected gain for the three groups, in the same order.

But comparisons by averages may be misleading, since a few extreme figures may unduly influence the results. It is important, therefore, to

TABLE 4.—*Percentage of Children Making Expected Gains in Height and Weight by Dietary Groups*

Dietary Group	Total	Height				Weight			
		Expected or More		Less Than Expected		Expected or More		Less Than Expected	
		No.	%	No.	%	No.	%	No.	%
All children	107	70	65	37	35	72	67	35	33
Control	36	22	61	14	39	21	58	15	42
Milk	36	24	67	12	33	25	70	11	30
D milk	35	24	69	11	31	26	75	9	25

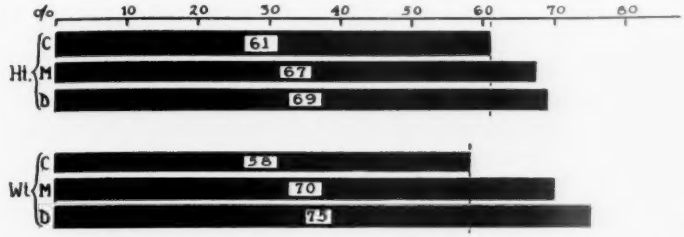

Chart 3.—Percentage of individual children in control group (*C*) and in groups receiving plain milk (*M*) and irradiated milk (*D*) who made their expected gain or better in height and weight (table 4).

consider also data for the individual children in the groups in respect to the item under consideration. In the present instance the expected gains for individuals show the same picture as those for the groups (table 4, chart 3). The percentages of children making their expected gains or more were 61, 67, and 69 for height, and 58, 70, and 75 for weight, respectively, for the control, the milk and the D milk group. This again shows an advantage for the groups receiving a supplement. Perhaps the most significant observation in these findings, however, is that a relatively large proportion of children in all groups failed to make even their normal gains in either height or weight during the year. This point will be discussed later.

GAINS OF INDIVIDUALS IN MATCHED TRIOS

Further comparison should be made on the basis of the matched trios. It will be recalled that the children in the three dietary groups were matched as well as possible at the outset on the basis of age, sex,

underweight and other significant factors. Of these original pairs, 24 remained complete throughout the year, and there were 9 other incomplete pairs consisting of a child from a control group and a child from one of the milk groups. The records of growth of these matched children have been examined to determine which of the 3 children (control, milk or D milk) in these trios made the best progress. A summary of these comparisons is given in tables 5 and 6 and in chart 4. It is of interest to note that for weight the control child made the best gain in only 12 per cent of the trios while the child given milk was best of the 3 in 46 per cent and the child given D milk in 42 per cent of the comparisons. In 63 per cent of the trios, moreover, both of the children receiving milk were superior to the control. For height the differences tended in the same direction, though they were not quite as marked.

One of the children given milk was best in 70 per cent of the comparisons, and both of them were better in 50 per cent of the trios. The 9 incomplete trios also showed a consistent tendency for the gains of

TABLE 5.—*Number of Times Annual Gains in Height and Weight of Each Dietary Group Ranked First, Second and Third in Twenty-Four Matched Trios*

	Height						Weight					
	First		Second		Third		First		Second		Third	
Group	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Complete pairs 24												
Control	7.0	30	4	16	13.0	54	3	12	5.5	23	15.5	65
Milk	8.5	35	8	33	7.5	31	11	46	10.5	44	2.5	10
D milk	8.5	35	12	50	3.5	15	10	42	8.0	33	6.0	25

the children given milk in both height and weight to exceed those of the control children. If we consider both first and second places in the trios, the results are even more in favor of the children who received a supplement. The child receiving milk was either first or second in 68 per cent of the comparisons for gains in height and in 90 per cent of those for weight; the child given D milk was first or second best in 85 per cent for height and in 75 per cent for weight. In contrast, the control child was poorest of the 3 in 65 per cent of the comparisons.

To a considerable extent, moreover, the best gains in height and weight were made by the same children. Table 6 shows that the child given milk was first in size of gains for both height and weight, or first in one and second in the other, in 38 per cent of the comparisons; the child given D milk in 46 per cent, and the control child, in 21 per cent. Conversely, the child given milk gained least in both height and weight in 8 per cent, the child given D milk in 4 per cent, and the control child in 42 per cent of the trios. The child given milk was better than the control child in 60 per cent of the groups and the child given D milk in 46 per cent; while the control group was better

than the milk group in both height and wieght in 30 per cent, and better than the D milk group in both in 21 per cent, of the trios. The results of comparisons of matched trios are thus found to be consistent

TABLE 6.—*Number of Times Gains in Both Height and Weight Ranked First, Second or Third for Each Dietary Group in Twenty-Four Matched Trios*

	Control		Milk		D Milk	
	No. Times	%	No. Times	%	No. Times	%
Best gains in both height and weight	2	21	6	38	5	46
Best in one, second in the other	3		3		6	
Best in one, third in the other	3		4		2	
Second in both	2	37	5	54	5	50
Second in one, third in the other	4		4		5	
Third in both	10	42	2	8	1	4
Better than control in both height and weight			14	60	11	46
Better than child given milk in both height and weight	3	12			8	33
Better than child given D milk in both height and weight	5	21	7	30		

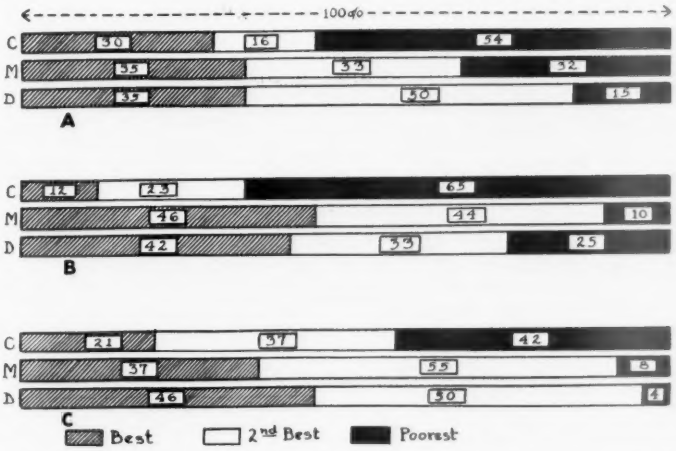

Chart 4.—Percentage of times control group (*C*) and groups receiving plain milk (*M*) and D milk (*D*) made best, second best and poorest gains. *A* represents gain in height, *B*, in weight and *C*, in both weight and height.

with those obtained by other methods of analysis; they offer supporting evidence that the differences in growth between the groups given a supplement and the group not given a supplement is due in part, at least, to the supplement of milk.

COMMENT

If one examines the charts, which show graphically the difference in gains in height and weight of the three dietary groups by various methods of comparison, it seems obvious that the groups given a supplement made measurably better progress during the year than did the

control group, which received the usual institutional diet. The differences for mean gain in weight are of the same order as those of Mann for English boys; those for height are not as great. The mean gain of groups may of course be misleading, unless the children in the several groups are in the same period of growth. If one group, for example, contains several children of the age in which annual gains of from 10 to 12 pounds (4.5 to 5.4 Kg.) are normal and the others do not, this might be sufficient to give misleading results. This source of error has been ruled out as fully as possible in this study by having the three groups matched for age and sex. Even this of course cannot fully assure comparable groups, for individual children may vary markedly in their patterns of growth. It is unlikely, however, that all children varying either negatively or positively from the standard for their age could by chance be put in the same group, thus vitiating the results to an extent as great as the differences found in this study. Since the differences are statistically significant for height and are in the same direction and approach significance for weight, they are probably real differences.

The comparison of actual gains with expected gains is perhaps fairer, especially in groups not perfectly matched, for each child's progress is judged by what is normal, on the average, for his age, sex and type of build. These expected gains are of course statistical averages, and no child would be necessarily expected to gain precisely the norm for his age. It is the only comparison possible, however, and since the standard is applied impartially to all groups it is probably as reliable as any available for assessing gains. The fact that the three groups gained, respectively, 6, 17 and 15 per cent more than the expected amount in height, and 9, 22 and 18 per cent more than the expected average in weight, indicates some superiority in favor of the milk groups. It is apparent, further, that these excessive gains were contributed by only a part of the children in the several groups; for 39 per cent of the control, 33 per cent of the milk, and 31 per cent of the D milk group failed to make even the expected gains in height, and 42, 30 and 25 per cent, respectively, gained less than the expected weight. This bears out a point which will be developed more fully in the later papers: that the experimental group as a whole was below average in development, and that the diet, even with the supplement, was still below the optimum in many respects.

The difference between the group receiving irradiated milk and that given nonirradiated milk is not consistently in favor of either. In some comparisons the milk group has a slight margin, in others the D milk group. In no case are the differences of the same order of size as the difference between both groups given a supplement and the control group. It seems justifiable to conclude, then, that the diets

were lacking in some or all of the constituents of milk, and that either there was no deficiency in vitamin D, or the 70 units provided by the milk was not enough to produce measurable results under the conditions of the study. This point will be further discussed in a succeeding article, dealing with development of bone.

Two variables that should be taken into account in interpreting the results are the percentage of milk consumption and the incidence of colds and other illnesses. Although all children in a given age group had access to the same amount of milk, the actual amount ingested varied somewhat, owing to occasional short absences from the institution, to illness, or to failure on certain days to take the full quota. A

TABLE 7.—*Percentage of Available Milk Taken by the Two Groups Given a Supplement*

Percentage of Milk	Milk Group		D Milk Group	
	Number	Per Cent	Number	Per Cent
90-99	18	50	16	46
90-95	11	30	9	25
85-90	4	11	7	20
Less than 85	3	9	3	9
Less than 60	..	..	2	..

TABLE 8.—*Days of Illness from Specified Causes for Each Dietary Group During the Year*

Group	Total Children	Colds, Influenza		Infectious Diseases		Inoculations		Miscellaneous		Total	
		Total	Average	Total	Average	Total	Average	Total	Average	Total	Average
Control	36	143	3.9	136	3.7	38	1.05	104	2.8	421	11.6
Milk	36	116	3.2	159	4.4	48	1.33	94	1.9	417	11.5
D Milk	35	151	4.3	155	4.4	26	0.74	60	1.7	392	11.2

daily record of milk consumption shows (table 7) that a somewhat larger percentage of the milk group received the greater part of the milk allotment than of the D milk group; 50 per cent of the milk, as against 46 per cent of the D milk group, ingested 95 per cent of the quota, and 80 per cent of the milk as compared with 71 per cent of the D milk group had 90 per cent or more of the allotment. Two of the children given D milk received less than 60 per cent of their milk, while no child in the plain milk group received as little as this. These differences in actual consumption may account in part for the slightly more favorable results in some comparisons for the plain milk group.

In the matter of illnesses there is little difference among the three groups (table 8). Although for some types of illness the groups differ, the average number of days for all illness is remarkably alike in the three groups: 11.6 days for the control, 11.5 days for the milk

and 11.2 days for the D milk group. This is a fairly high average for all groups, and it may help to explain the failure of so large a percentage of the children to make even their expected gains.

When the excellence of the supplement is considered, it seems at first thought surprising that the gains of these children were not greater. When the full pint equivalent of milk was taken, it contributed generous amounts of a number of dietary constituents and supplemented many of the deficiencies of a diet which was too largely carbohydrate. That greater gains were not secured may probably be attributed to the fact that, as already indicated, the diet was still low in some of the dietary essentials. This point will be shown more fully later, when the analysis of the dietary study is reported. Gains of even the size attained, however, are far from negligible for a year's time.

SUMMARY

The growth of three groups of institutional children, consisting of 36 children each, was followed throughout a calendar year. One group remained on the usual institutional diet as the control; one received daily an additional pint equivalent of evaporated milk and one an equal amount of irradiated evaporated milk.

By all methods of comparison the growth of the children given a supplement exceeded that of the controls. The average excess in mean gain in height was 0.9 cm. (0.3 inch) for both milk groups, and in weight was 1.03 Kg. (2.27 pounds) for the plain milk and 0.62 Kg. (1.4 pounds) for the irradiated milk group.

The percentages of expected gains made by the three groups were 106, 117, and 115 for height and 109, 122, 118 for weight for the control, the plain milk and the irradiated milk group, respectively. The percentage of individual children in these groups who made expected gains or better was 61, 67, and 69 for the height, and 58, 70, and 75 for the weight of the three groups, in the same order.

When comparison was made of the gains of the individual children in 24 matched trios, the gains in weight of the control child were best in 12 per cent, of the child given plain milk in 46 per cent, and of the child given the D milk in 42 per cent of the trios. The gains in height were in the same order but were less marked.

Though the differences are not large and do not always attain statistical significance, they tend consistently in the same direction by all methods of comparison and probably represent real differences which can be attributed in part, at least, to the dietary supplement.

The expenses of this investigation were defrayed in part by the Irradiated Evaporated Milk Institute.

STRIAE IN THE BONES OF A SET OF MONOZYGOTIC TRIPLETS

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AND
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Transverse striations in the ends of the long bones of children have been described by Eliot, Souther and Park,[1] Phemister,[2] Kohler,[3] Wegner,[4] Sontag [5] and others. Apparently they may result from any one of a variety of factors. Broad, heavy striae seen on roentgenoscopic examination most frequently result from lead or phosphorus poisoning. Narrow lines resembling pencil marks and often traversing only a part of the width of the bone are seen much more frequently than are the broad bands and are believed to result from periods of cessation of growth, illness, rickets or hypervitaminosis D. In our serial studies of a large group of children at the Fels Research Institute we believe that we have observed these lines after periods of accelerated growth as well. In some instances we have been unable to observe, by means of careful anthropometric measurements, measurements of bones and physical examinations, any evidence of a period of decelerated growth or of illness preceding the period of acceleration which seemed to produce the striae. Eliot, Souther and Park [1] have made a careful study of the formation of striae in the bones of rats. They have correlated their histologic findings with their roentgenologic findings. They have described the histologic appearance of the fine white line seen in the roentgenogram as a transverse lattice formation of bone. They suggested that it has its origin at the junction of the shaft and the cartilage and results from a sudden retardation or cessation of the growth of the cartilage, which causes the bone-building energy of the shaft to con-

From the Samuel S. Fels Research Institute of Antioch College.

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centrate at a single level or at slowly changing levels and to discharge itself in a more lateral direction. When the growth of the cartilage becomes reestablished, trabeculae with the ordinary parallel longitudinal arrangement form again, leaving the previously formed lattice work behind. Eliot, Souther and Park questioned whether these lines are caused by the provisional or temporary zone of calcification, because rickets, in which there is a dearth of mineral in the temporary zone, frequently causes such lines. This reasoning may or may not be correct. It must be remembered that while there is during active rickets a depletion of mineral in the bone and in the temporary zone of calcification, one of the first evidences of the healing of a rachitic bone occurs at the temporary zone of calcification, which rapidly becomes abnormally thickened and heavy. The striae which are seen after rickets may therefore be the result of the healing process rather than of the active process and may result from the overdevelopment of the temporary zone during this healing.

Despite differences of opinion as to the mechanism, it is generally agreed that, aside from rickets, the usual cause of the formation of fine osseous striae is retardation of growth from known or unknown causes. Illness of sufficient severity is capable of producing striae but probably does so through the medium of cessation of growth. We have observed striae that appeared to follow severe emotional disturbances (again, probably occurring through the medium of retardation of growth). It has seemed to us that a careful study in which illness and the rate of growth are observed in relation to the appearance of striae may help to clarify the causation and significance of striae.

In order to eliminate the possibility of differences in stria formation which might be due to inherent differences in the germ plasm, we selected for our studies a set of monozygotic triplets, now 9 years old, who have been under observation at the Samuel S. Fels Research Institute for the greater part of their lives. Evidence of their uniovular origin has previously been published (Sontag and Nelson [6]), as has a description of their behavior differences (Sontag and Nelson [7]). The uniovular origin of these triplets has assured us that the differences in the number and location of the striae and the differences in their rates of growth are not due to hereditary differences, as they might be in siblings or unrelated children, but must be due to variations in the severity of illness, quality of nutrition and environmental influence.

In this study the criterion for recording the presence of a stria was based on its length. Striae which traversed one half or more of the width of the bone were used. Such a standard is obviously somewhat arbitrary, but it is, never-

6. Sontag, L. W., and Nelson, V. L.: Study of a Set of Identical Triplets: I. Comparison of Physical and Mental Traits of a Set of Monozygotic Dichorionic Triplets, J. Hered. **24**:473 (Dec.) 1933.

7. Sontag, L. W., and Nelson, V. L.: Study of a Set of Identical Triplets: II. Behavior of a Set of Identical Triplets, J. Genetic Psychol. **42**:406 (Dec.) 1933.

theless, one commonly used. In instances in which a stria was qualified for inclusion by its length at one age level but in later roentgenograms was seen to have faded so as to cover less than half the shaft, its length at both age levels was recorded and used. The proximal and distal ends of the tibia and fibula and the distal ends of the femur and radius of the left side of the body were studied.

In several instances in which striae in one or perhaps two bones were indicated, partial striae, corresponding in time of formation, were found in some or all of the other bones; such striae, however, were not recorded, because they traversed less than half the width of the bone. The depth of the stria was always measured from the end of the bone along the central longitudinal axis. Striae are indicated in the diagrams by small circles, and their depth or distance (in millimeters) from the end of the bone is shown by the scale at the left labeled depth of stria. Roentgenograms were made at the ages of 28, 36, 42, 48, 54, 60, 66, 72, 78, 84 and 96 months. The determination of the time of formation of the striae by projecting them on the base line is, of course, subject to some error. Projection was done, whenever possible, by identifying individual striae at two or three ages, indicating the position of these striae in the figure and drawing a straight line through them to the base line. Projection of other striae at the same age level and in the same bones was then made parallel to them. Such a process is subject to the possible error of misidentification of an individual stria at two different ages and to changes in the rate of growth between the time of formation of the stria and its initial appearance in the ray, as compared with its rate of growth between its first and second appearance. The first error is rather unlikely, since this method was used only when the spacing of the striae or their unusual heaviness was such that they could readily be identified at two different age levels. When an individual stria or group of striae could not be positively identified at two different age levels so as to determine the slant of the projection line, this slant was determined by a study of the increment of growth of that bone from the previous age level. This method also is subject to some error, since growth takes place at both ends of a bone; and, while known relative rates of growth for the two ends of a bone were used in the calculations, they were determined from averages and are, of course, subject to some individual variation.

Because of the source of error described, we make no claim that the vertical lines in the charts representing the supposed time of formation of the stria in all instances represent the exact time of formation. The most we can say is that they approximate it.

COMMENT

It will readily be seen from the charts that in each of the 3 children the striae were arranged in four groups. The only exception which might be noted is in the case of John in which the last two groups coalesced. Such a situation might suggest that a hereditary factor was responsible for the formation of striae. Further inspection, however, reveals that in the number of striae and the period of time during which they were laid down, John was far ahead of the other 2 children. An examination of all three charts indicates at once that there is no single cleancut and apparent etiologic factor common to the production of all of the striae.

RESULTS

John (chart 1).—John had more striae and striae distributed over a longer period than had either of his brothers. He had the same illnesses as his brothers, and, as far as could be determined, these were of comparable severity. His growth curve was not appreciably more irregular in regard to either gain in height or gain in weight. It is

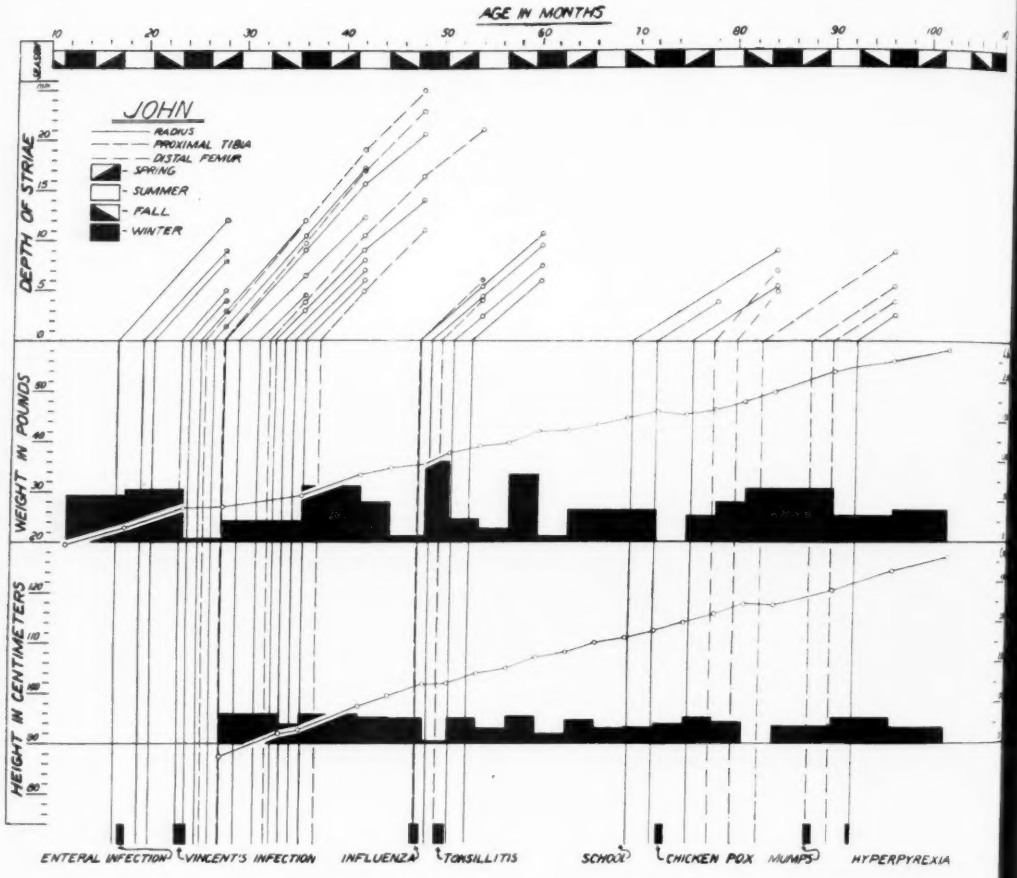

Chart 1.—Diagram showing the location and projection of striae in the long bones of John in relation to time, seasons, changes in rate of growth, illness and entry into school.

possible, of course, that the three month intervals at which height and weight were ascertained included far too long a period and that a constant record might present a much more irregular or "saw-tooth" appearance, owing to short rest periods and spurts of growth.

John's first group of striae, containing those laid down between the ages of 12 and 40 months, certainly cannot be traced directly to the two minor illnesses suffered during that period. His gain in weight

from 24 to 28 months was slight, and that period showed the formation of unusually heavy striae. The ensuing eight months showed a slightly more rapid gain in weight, but one that was still slow compared to that of other periods in his life. This total period between the ages of 24 and 36 months, when the gain in weight was below average, included the time of appearance of most of the striae in the first group. He gained slightly less during this period than did either of his brothers. There was an emotional factor which may have been responsible for both the small gain in weight and the excessive number of striae found during this period. It was in the period extending between the ages of 18 and 40 months that John showed definite emotional instability, manifesting itself in an unusual attachment for his mother and a tendency to avoid contacts with other children. He was, during this period, clearly his mother's favorite. Competition with his brothers for his mother's interest and attention was both apparent and successful. He became hypersensitive, cried for toys instead of taking them, as did his brothers, and managed usually to gain his ends by eliciting his mother's interest and help rather than by fighting.

The importance of such a period of emotional stress in the production of these striae in the bones is, of course, entirely problematic. The disturbing effects of emotional stress on metabolic processes and nutrition are, however, frequently seen, and it does not seem improbable that they may be shown, in the case of John, by the extensive formation of striae. We have noted in other instances a single heavy stria in the long bones of children apparently following a sudden emotional shock.

The second group of John's striae conformed well with the incidence of acute infectious processes and with a period of fluctuant growth. The causes of the third and fourth groups are not clear. Three illnesses occurred during their formation, and during the formation of the third group John spent his first year in a strict parochial school. The fourth group seemed to conform in time to an attack of mumps and to a fever of unknown origin.

Fred (chart 2).—Fred's first group of striae were formed over a much shorter period than were John's and were much fewer. They were formed principally during a period of slight gain in weight and a period of no increase in height.[8] The first of the group were laid

8. The decrease of 3 cm. in Fred's height at the age of 45 months as compared with his height at 42 months is primarily due to an error in measurement at 45 months. This measurement was made by a new member of the staff, who was at that time just learning anthropometric technic. Through an oversight, her measurements on this occasion were not checked. It is possible that differences in the hour of the day at which the measurements were taken contributed a part of the error. Henry shows a similar but less marked decrease in height at the same age level.

down during a winter when his general level of physical well-being was not high. It is possible that the Vincent's infection, which was severe and prolonged, interfered enough with his eating habits to have had an effect. The formation of the second group corresponded in time to periods of infectious disease and to periods of low growth increments. The third group of striae were formed during a winter when he had

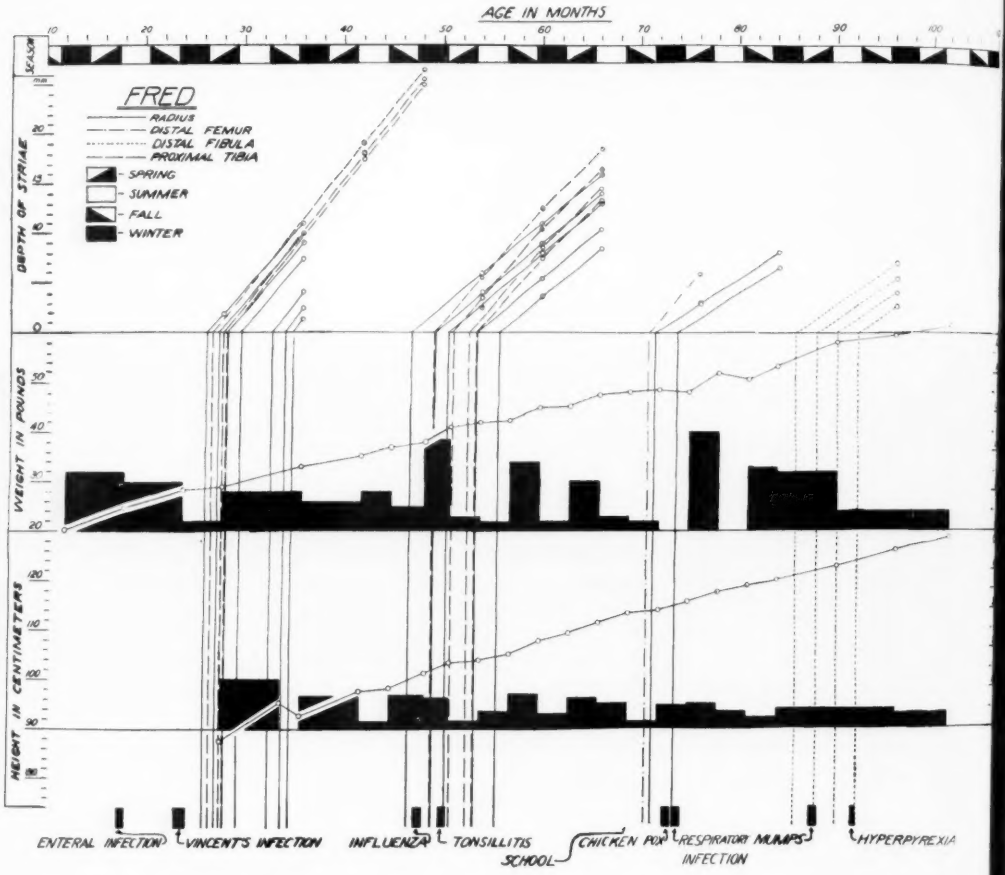

Chart 2.—Diagram showing the location and projection of striae in the long bones of Fred in relation to time, seasons, changes in rate of growth, illness and entry into school.

chickenpox and colds in the chest and had to make his adjustment to school. The fourth group, although somewhat disseminated, were associated with mumps and with fever of unknown origin.

Henry (chart 3).—Henry's first group of striae closely resembled those of Fred. In this instance, however, the second half of the group did not conform with a period of much retarded growth. These four

striae were found during the summer months, and it is possible that these, as well as those of Fred and John that were comparably placed, may have resulted from a sudden increase in vitamin D as a result of exposure to sunshine.

Henry's second group conformed well with a period of no increase in height and with acute infectious disease. The third group conformed

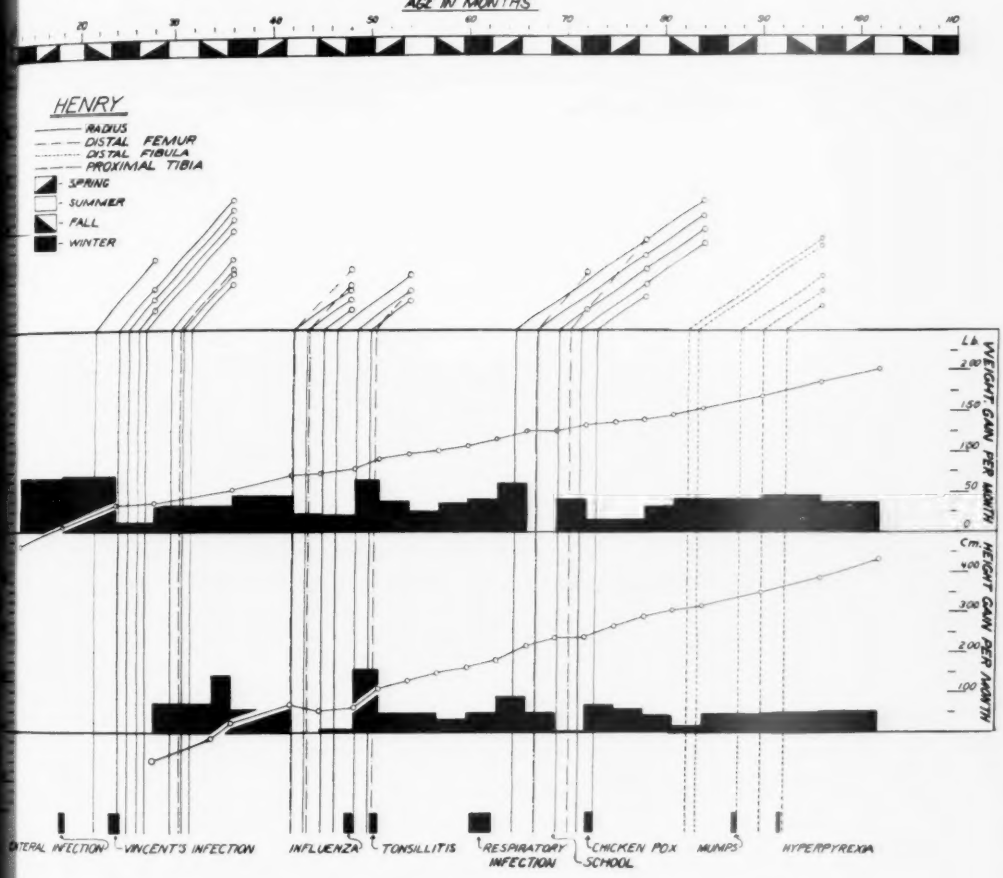

Chart 3.—Diagram showing the location and projection of striae in the long bones of Henry in relation to time, seasons, changes in rate of growth, illness and entry into school.

in time of formation with periods of disturbance in his gain in height and weight, with an attack of chickenpox and with entry into school. The fourth group of striae were somewhat divided, the first stria falling on a period of slow growth in height and the second on the occurrence of mumps and of fever of unknown origin.

SUMMARY

We have presented diagrams showing the occurrence of striae in the long bones of each of a set of identical triplets. We have projected these striae so as to determine as closely as possible the period during which they were formed. In order to study their possible causes we have included in the diagrams data regarding such factors as height, weight, increments of height and weight, season of the year, illness and entry into school. While there was some similarity in the occurrence of striae in these children, there were enough differences to indicate that the hereditary factor is not the only one, if indeed it is a factor at all, in the formation of striae. We have suggested that such factors as illness, periods of retarded growth in height and weight, increased intake of vitamins and emotional disturbances may have played a part in the formation of striae in the long bones of these triplets.

We have presented this study not with the wish arbitrarily to assign causes for the striae in the bones but to show the location of the striae in relation to possible etiologic factors, in the hope that such a presentation may aid others, as it has aided us, in a better understanding of striae.

Physical measurements and histories of the triplets were taken by Drs. D. Snell, G. Shong, A. Hunter and M. Singer. Measurements of striae were made by S. I. Pyle, George Comstock and L. W. Sontag.

BASAL METABOLIC RATE OF YOUNG CHILDREN WITH NEPHROTIC SYNDROME

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The basal metabolic rate of patients with nephrosis has been reported as low in the majority of instances.[1] However, few data are available on young children with the nephrotic complex. The present studies were carried out in the process of making certain other detailed observations on the children concerned, without regard to their clinical condition at the time.

CONDITIONS OF OBSERVATION

All the patients were in the Hospital of the Rockefeller Institute for Medical Research while these observations were made. All presented well defined evidences of the nephrotic syndrome, as manifested by edema, lowered level of albumin in the plasma with reversal of the albumin-globulin ratio, absence of hypertension, lack of retention of nitrogen and definite albuminuria without hematuria. More complete data on the metabolism of some of these children from other aspects have already been reported.[2] No attempt will be made here to separate the patients into a group with the so-called pure lipoid nephrosis and

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From the Hospital of the Rockefeller Institute for Medical Research.

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2. (*a*) Page, I. H., and Farr, L. E.: The Influence of High and Low Fat Diets and Thyroid Substance on Plasma Lipids of Nephrotic Patients, J. Clin. Investigation **15**:181 (March) 1936. (*b*) Farr, L. E.: The Effect of Dietary Protein on the Urea Clearance of Children with Nephrosis, ibid. **15**:703 (Nov.) 1936; (*c*) The Assimilation of Protein by Young Children with the Nephrotic Syndrome, Am. J. M. Sc. **195**:70 (Jan.) 1938.

one with the nephrotic type of chronic glomerular nephritis. No useful purpose could be observed by any arbitrary distinction in the absence of quantitative objective data supporting the classification, nor has any evidence been uncovered in our studies of these children which would make it likely that such a separation would have any value for the purposes of this paper. These children represented a highly selected group of patients, as all were referred to this hospital because they were believed to have genuine nephrosis.

Throughout the periods of observation they were all given comparable weighed diets, and there were no known complicating factors at the time the tests were made: That is, the children showed no clinical evidences of infection and were afebrile.

The children were not given any sedative prior to the tests, since this was found to be unnecessary with the regimen used. Before any tests were made, the youngest were each given a fitted rubber mouth piece as a plaything. This was repeatedly fitted into the child's mouth, so that he had no fear of that procedure. After this step had been taken, the mouth piece was put in place, and the nose was held for short periods to accustom the child to breathing through the mouth piece. After he became thoroughly acquainted with this regimen, he was shown the spirometer, and for a short period a test was made. On the following day it was usually possible to make a series of duplicate tests before breakfast, just after the child awakened. These were usually satisfactory the first time, and thereafter the complete cooperation of the child was assured. The remarkable response of these children to quiet suggestion enabled results to be obtained which agreed much more closely than was originally expected. The average set of duplicate analyses for these young patients agrees as well as those obtained for adults who were used to such manipulations. With some of the children it was necessary to screen the machine after the tests became an old story, for they found a source of never ending amusement in deliberately breathing deeply to make the spirometer rise and fall; but with the instrument screened from sight the game lost its zest, and the results checked in a satisfactory manner. In general, the children were observed at irregular intervals whenever for one reason or another it became desirable to measure the basal metabolic rate. Once they were trained to the routine, there was no difficulty in subsequent tests.

CALCULATIONS

The results were calculated as cubic centimeters of oxygen consumed per minute. This was derived as calories by using the factor 1 liter of oxygen $= 4.825$ calories. Surface area was calculated from Du Bois' formula as $A = \frac{Ht.^{0.725} \times Wt.^{0.425} \times 71.84}{10{,}000}$, the height being given in centimeters, the weight in kilograms and the surface area in square meters. Basal metabolic rates were calculated from the data of Lewis, Kinsman and Iliff, and ideal weights, which were used throughout in calculating surface area, were obtained from the tables of Woodbury, Baldwin and Wood.

Ideal weights rather than actual weights were used at all times for calculating surface area, on the assumption that the amount of active metabolic tissue remained relatively constant without regard to edema. The actual weights would have introduced serious errors at times when the children were exceedingly edematous. Since the retained salt and water play no part in consumption of oxygen, an erroneous observation would thereby be introduced by including them in the metabolizing body weight. Further justification for the choice of these ideal weights is to be found in this fact: With recovery from edema and also

from the disease the children rapidly approached the ideal weights so closely that no error was introduced by using the values obtained during the non-edematous state rather than the actual weights.

RESULTS

Thirty-four tests made for 8 patients showed no significant deviation from the expected metabolic rates, with one exception. The results are summarized in the accompanying table. In every instance duplicate tests were made, and the data here given are the averages.

Representative Determinations of the Basal Metabolic Rate for Seven Nephrotic Children

Patient	Sex	Date	Age in Years	Basal Metabolic Rate, Deviation from Standard Percentage
I. C.	F	2/ 7	3.75	— 1
		2/11		+24
		3/27		+13
		3/30		+ 2
		5/30	4.00	+16
		9/18	4.50	— 4
		9/28		+12
J. F.	M	11/ 3	6.25	—12
		11/10		—19
		2/ 2	6.50	+ 9
		2/11		+35
		3/28		+10
		5/18	6.75	— 1
		5/27		+ 8
J. M.	M	10/18	3.75	+ 6
		2/ 6	4.00	+ 8
		2/11		+11
		3/26		+ 2
		5/18	4.25	+ 8
		5/29		+15
		9/17	4.50	+14
		9/24		+15
T. M.	F	3/27	3.00	+ 6
		5/15	3.25	— 3
		5/28		+ 6
E. S.	F	9/21	4.00	+ 8
		9/27		+ 9
H. R.	M	9/19	3.75	Normal
		9/23		+11
J. T.	M	9/ 4	4.50	+ 8
		9/23		+ 1

It is interesting that in no instance was a consistently low basal metabolic rate obtained, whereas for 1 patient (J. M.) the basal metabolic rate seemed to be increased. This patient appeared to have genuine nephrosis. In studies reported elsewhere [2a] he did not show increased tolerance to thyroid, nor was he benefited by it. The cause for the apparent elevation of his basal metabolic rate could not be ascertained. One difficulty in interpreting these tests arises in the selection of suitable standards. The standards used were those reported for American chil-

dren by Lewis, Kinsman and Iliff [3] and were selected because they give data on very young as well as on older children.

SUMMARY

Basal metabolic rates of 8 children with the nephrotic syndrome were measured. In none was a consistently lowered basal metabolic rate found, using the standards of Lewis, Kinsman and Iliff. In 1 case a slightly but consistently elevated rate was noted.

3. Lewis, R. C.; Kinsman, G. M., and Iliff, I.: Basal Metabolism of Normal Boys and Girls from Two to Twelve Years Inclusive, Am. J. Dis. Child. **53**: 348 (Jan.) 1937.

Case Reports

CONGENITAL CILIATED COLUMNAR EPITHELIAL CYSTS OF THE MEDIASTINUM

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Only occasional reports of congenital ciliated columnar epithelial cysts of the mediastinum are found in the literature of the past fifty years. A fairly extensive review reveals that less than twenty proved cases are reported in the English and the German literature, most of these in the latter. Undoubtedly there have been many unreported cases. These cysts are benign, and since the mediastinum is becoming more accessible, owing to rapid advances in surgery of the chest, the future should offer more hope for patients with this condition.

The following case presents a typical example of this kind of cyst.

REPORT OF A CASE

History.—A 7 month old girl was admitted to the pediatric service of the Vanderbilt Hospital on Oct. 8, 1936, and died eight hours later. She was the second child, the result of a normal pregnancy. At delivery the cord was twisted about the neck three times; at first the baby was considered dead, but with much stimulation she was resuscitated. Since birth she had had noisy and labored breathing spells with cyanotic attacks when she cried. These were worse in the first two months, but they continued, at about the rate of one spell per week, until the week prior to admission, when they became more frequent and much more severe. The child had fever and took her feedings poorly. She was breast fed for the first two months and then took cow's milk. There was no history of aspiration of a foreign body.

Physical Examination.—On admission the child's temperature was 102.8 F., the pulse rate 148 and the respiratory rate 40. She was obviously very sick. She was undernourished and underdeveloped. The respirations were difficult, with harsh rattling and some retraction. The face was ashen, and there was circumoral pallor. The skin was pale and elastic, and there was no superficial glandular enlargement. There was slight bossing of the head but no craniotabes. The anterior fontanel was soft and measured 2.5 by 1.5 cm. There was a mucoid discharge from the nose, and the throat was diffusely red. The trachea deviated to the left. The left side of the chest was smaller than the right and moved less on respiration. Anteriorly there was resonance from the right side over to the left nipple line. On the left, the breath sounds were rather distant and high pitched; at the end of inspiration there were fine rales, and on expiration there were extremely harsh breath sounds. The point of maximal impulse of the heart

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was not made out. The heart sounds were maximal in the left axilla. The rhythm was regular, and no murmurs were heard. The remainder of the physical examination gave entirely negative findings.

Course in the Hospital.—The patient did not take feedings properly, and an attempt at gavage was unsuccessful. As soon as the tube was passed down the esophagus she became dyspneic and deeply blue. When the tube was withdrawn she vomited a small amount. Administration of mechanical stimulation, suction, carbon dioxide and oxygen, a solution of epinephrine hydrochloride and atropine brought slight temporary improvement. Rales were heard at this time on the right side of the chest. Results of the laryngoscopic examination were essentially negative. Respiratory difficulty increased, and the patient died three hours after the attempted gavage and eight hours after she entered the hospital. No laboratory work was done. A roentgenogram made elsewhere before admission was said to show atelectasis of the left lung but no mediastinal mass.

The central nervous system was not examined at autopsy because of restrictions in the permit. Except for this, a complete gross and microscopic examination was performed, but only the pertinent facts are included in the following account.

Autopsy Report.—Gross Examination: When the skin was resected from the thoracic wall the right side of the chest appeared definitely larger than the left, and the intercostal spaces on this side were wider. Water was poured into the angle between the wall and the skin resected from the right side; then a puncture was made below the surface of the water into the right pleural cavity. When pressure was applied on the anterior surface of the chest, a few bubbles of air passed through the water, indicating pneumothorax. A needle was inserted through the interspace, and 20 cc. of air was easily removed from the right pleural cavity. There was about 150 cc. of clear fluid in this cavity. The pleural surfaces on the left were covered with a fibrinopurulent exudate, which was most marked about the diaphragmatic surface. There was no fluid in the left cavity.

The pericardial surfaces were smooth and glistening and had no connection with the cyst. The thymus was large, weighing 19 Gm. and extending down on the anterior surface of the pericardium. It appeared normal in consistency and had no gross hemorrhage, necrosis or cyst formation.

After the heart and lungs were removed a mass was seen between the trachea and the esophagus. The upper edge of this mass was 1 inch (2.5 cm.) above the bifurcation of the trachea. It measured 5 cm. in diameter; it had a thin wall and fluctuated readily. While the cyst was being dissected out, the wall was incised, and about 15 cc. of clear, watery mucoid fluid poured forth. The mass pressed on the left bronchus and on the lower end of the trachea in such a way as to flatten out these tubes. The left bronchus was compressed so much that it was creased along its left border. This obstruction of the left bronchus was sufficient to cause complete atelectasis of the left lung. There was no definite obstruction of the right bronchus. Careful inspection of the cyst revealed no communication with surrounding tissues. The sac was attached to the trachea by a small stalk of fibrous tissue, which seemed more dense than the small tags of fibrous tissue which held the cyst loosely to the surrounding tissues elsewhere. The inside of the sac was smooth and had no partitions, papillomatous growths or evidence of inflammation.

There was no food or foreign body in the larynx, trachea or bronchi. The thyroid and esophagus were normal.

The right ventricle of the heart was slightly dilated.

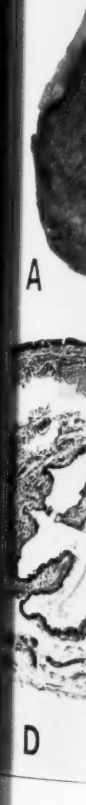
The right lung weighed 65 Gm. and the left 80 Gm. The right lung was partially compressed by a hydropneumothorax. About half of the upper lobe was noncrepitant and had the meaty consistency which characterizes atelectasis without consolidation. Careful search revealed no break in the serosa which might explain the air in the right pleural cavity. The left lung had fibrinopurulent exudate on the surface. In addition to complete atelectasis, there was irregular, nodular consolidation, which indicated bronchopneumonia. On the lateral surface of the lower lobe there was a small break in the pleura over an area of consolidation which was apparently the source of a slight amount of hemorrhagic exudate. There was a softness in this area of consolidation which indicated early abscess formation; its contact with the pleura suggested that this abscess was the source of the pleuritis. There was purulent exudate in several of the bronchial tubes of this lung. As already mentioned, there was obstruction of the bronchus on this side by the cystic mass in the mediastinum. The mediastinal nodes were not enlarged. The remainder of the gross examination showed nothing of note.

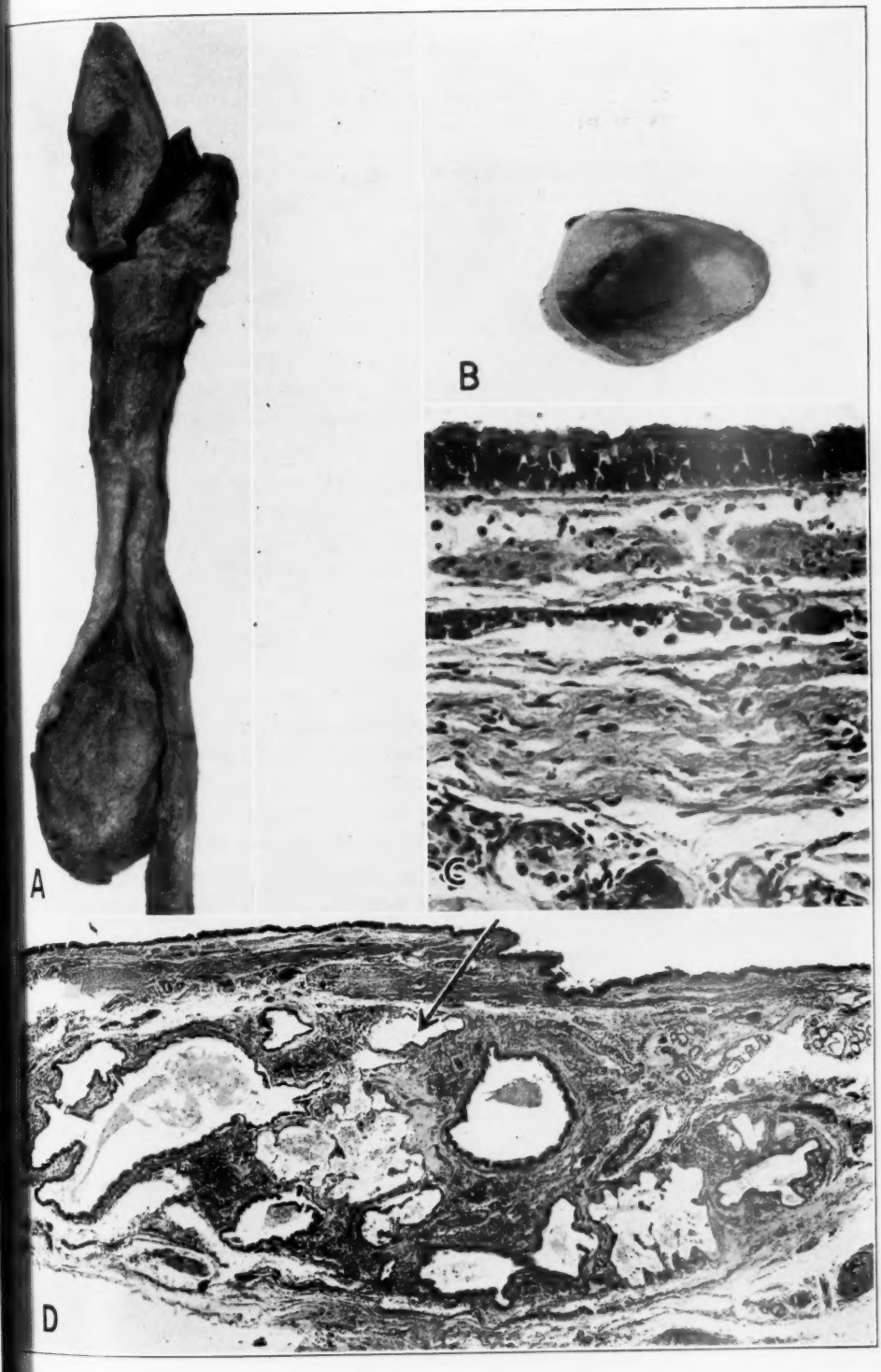
Microscopic Examination: One section from the upper lobe of the right lung showed complete atelectasis without any inflammatory change, while one from the lower lobe showed only partial atelectasis, with focal areas of hemorrhage. The pleura of the left lung was covered with a thick layer of fibrinopurulent exudate. Sections of this lung showed atelectasis associated with acute, confluent bronchopneumonia, as indicated by the abundant exudate of polymorphonuclear leukocytes in the bronchial tubes and in the partially collapsed alveoli. Some of the alveoli contained considerable fibrin, and in several places a few young fibroblasts were growing into and organizing this alveolar exudate. In addition to the bronchopneumonia with early organization, there was subacute inflammation of the interstitial tissue. There were several hemorrhagic areas, approximately four times the size of a low power field, in which the structural elements of the lung were definitely necrotic. These areas represented early abscesses. There was no foreign material in these or in the bronchial tubes.

The cyst was lined almost entirely by ciliated columnar epithelium. In a few small areas there was cuboidal epithelium, and in such areas small foci of flattened pavement epithelium were seen. In several places the epithelium, with a narrow supporting stalk of fibrous tissue, projected into the lumen of the cyst, forming a finger-like villus. By means of connective tissue stains, small circular interrupted bands of smooth muscle were shown just beneath the epithelial lining of the cyst wall. In addition to a loose stroma of fibrous tissue throughout the wall, there were compact longitudinal bundles in which dense elastic fibers were present. The wall of the cyst contained smooth muscle, fibrous tissue, cartilage, mucous glands, blood vessels and nerves. All of these elements were arranged similarly to those in the wall of a normal bronchus, which at once suggested the bronchiogenic origin of such cysts. In the wall of the cyst was unmistakable evidence of attempts to form bronchial tubes and even alveoli. Several spaces were lined by ciliated columnar epithelium which was supported by a thin layer of fibrous tissue. One such structure, in which there was gradation to flattened epithelium, had a marked similarity to an alveolar duct. In this same region were delicate structures, lined with flattened epithelium, which had a marked resemblance to normal alveoli. Thus there were rudimentary bronchial tubes and lung tissue in the wall of the cyst. There was a subacute inflammatory reaction in the wall of the cyst; this was most marked about the mucous glands and rudimentary lung structures. The heart, liver, spleen, pancreas, adrenals and kidneys showed no significant microscopic changes.

LEGEND FOR FIGURE

A, left lateral view of the cyst, showing its relation to the trachea, the left bronchus and the esophagus. The compressed left bronchus lies on the upper anterior surface of the cyst. The esophagus lies posteriorly. *B*, a view of the interior of the cyst, which has been cut in two so as to show the thin wall and smooth lining. It was distended with clear, watery mucoid secretion. *C*, high magnification (× 225) of a section of the cyst wall, showing ciliated columnar epithelium beneath which are small interrupted bands of smooth muscle. In the lower half there is a longitudinal band of fibrous tissue. *D*, the cyst wall, showing rudimentary bronchial tubes and alveolar structures; × 20. The arrow points to a bronchiole which shows a transition from cuboidal to flattened epithelium; the structure resembles a normal alveolar duct. Such observations further substantiate the theory of the bronchiogenic origin of these cysts.




A
B
C
D

Summary of Pathologic Observations: The changes noted at autopsy were: congenital ciliated columnar epithelial cyst of the mediastinum, with pressure on the left bronchus and resulting atelectasis of the left lung; bronchopneumonia and early abscess formation of the left lung; beginning organization of exudate in the alveoli of the left lung; fibrinopurulent pleuritis on the left, an extension from the abscess beneath the pleura; hydropneumothorax on the right, unexplained, and partial atelectasis of the upper lobe of the right lung.

COMMENT

This child died eight hours after admission, before a complete examination, including laboratory procedures, was done. From the clinical findings it seemed most likely that there was a mediastinal mass pressing on the left bronchus and producing atelectasis of the left lung, in which there was superimposed pneumonia. Had the child lived, undoubtedly bronchoscopy would have confirmed the suspicion of compression of the left bronchus. Autopsy added little to the clinical diagnosis except the type of mass in the mediastinum.

As was suggested by the fact that intermittent attacks of dyspnea and cyanosis had persisted since birth, the cystic mass was congenital. Its lining of ciliated columnar epithelium and its wall, which contained mucous glands, cartilage, muscle, fibrous tissue and nerves, all arranged similarly to those in the wall of a normal bronchus, at once suggested the bronchiogenic origin. Indeed, in several places there appeared to be an attempt to form lung tissue in the wall of the cyst (fig. *D*). Reports in the literature support the theory that such cysts are of bronchiogenic origin. Gold [1] cited cases in which the cysts were noted in the lumens and in the walls of the bronchi. Further, since the walls of the cysts contained all the elements of a bronchial wall, arranged as in a normal bronchus, he concluded that the cysts arise from the trachea or from the bronchi. This view, which has been generally accepted by recent writers, contradicts the older hypothesis of Bert and Fischer (quoted by Gold [1a]), who maintained that in fetal life the esophagus is lined with ciliated columnar epithelium and that these cysts arise from the esophagus.

Probably the two most generally accepted theories of bronchiogenic origin are: (1) During fetal life there is imperfect closure of the communication between the respiratory passages and the esophagus. Such a communication usually has its site above the bifurcation of the trachea, and formation of the cyst may occur when the two ends of the communication close and the passage itself remains. (2) The cyst represents a rest pinched off from the trachea or from one of the bronchi.

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1. (*a*) Gold, E.: Ueber Bronchuscysten und deren Entstehung, Beitr. z. path. Anat. u. z. allg. Path. **68**:278-296, 1921. (*b*) Chiari, H., cited by Gold.[1a]

These cysts vary from a few [2] to several centimeters in diameter (Monti [3] reported one the size of a child's head). They contain watery mucoid secretion. Their walls are thin and often have two (inner and outer) layers of smooth muscle, cartilage, mucous glands and a lining of ciliated columnar epithelium. They are closely associated with the respiratory passages. Zahn [4] observed one along the cardiac end of the stomach which he thought arose from the esophagus. This is the only such case reported. Most of the cysts are situated near the bifurcation of the trachea, usually on its posterior surface. In most instances no remnant of a communication with the trachea or with the surrounding viscera is present.

Some of these cysts [5] produce no symptoms but remain quiescent and are noted only at autopsy. Others [6] produce symptoms of pressure on the trachea, bronchi, heart or great vessels. The most frequent symptoms are dyspnea, cyanosis and a brassy cough, but not infrequently there is palpitation. Since the cysts are congenital, the onset of symptoms is often at birth [7] or in early childhood; however, the symptoms may occur for the first time in adults.

DIAGNOSIS

As in the case reported here, often the roentgenogram shows no mass in the mediastinum but only atelectasis secondary to pressure on the air passages. Even when a mediastinal mass is found by roentgen examination, conditions which are seen more frequently, such as der-

2. Herrmann, K.: Ueber eine Flimmercyste des Mediastinums, Prag. med. Wchnschr. **15**:146, 1890.

3. Monti, R.: Flimmerepithelzyste des Mediastinums, Wien. med. Wchnschr. **75**:1802, 1925.

4. Zahn, F. W.: Virchows Arch. f. path. Anat. **143**:416-418, 1896.

5. Zahn,[4] Stilling, H.: Eine Flimmercyste des Mediastinum anticum, Virchows Arch. f. path. Anat. **114**:557-560, 1888.

6. (*a*) Fletcher, H. M.: A Congenital Cyst of the Mediastinum, Tr. Path. Soc. London **48**:249-251, 1896-1897. (*b*) Blackader, A. D., and Evans, D. J.: A Case of Mediastinal Cyst Producing Compression of the Trachea, Ending Fatally in an Infant of Nine Months, Arch. Pediat. **28**:194-200, 1911. (*c*) Rach, E.: Kompression des rechten Hauptbronchus durch eine Zyste, Wien. med. Wchnschr. **70**:37-38, 1920. (*d*) Bramwell, B.: Cystic Tumor in Anterior Mediastinum Simulating Aneurysm, Clin. Studies, Edinburgh **1**:145-147, 1902. (*e*) Mixter, C. G., and Clifford, S. H.: Congenital Mediastinal Cysts of Gastrogenic and Bronchiogenic Origin, Ann. Surg. **90**:714-729, 1929. (*f*) Sultan, G.: Bronchuscyste, Zentralbl. f. Chir. **52**:869-873, 1925. (*g*) Fletcher [6a] cited a case by Lannelongue and Achard similar to his. (*h*) Fletcher [6a] cited a case by Roth similar to his. (*i*) Alford, J. E.: Congenital Bronchogenic Cyst of the Mediastinum in an Infant, Arch. Path. **23**:296-297 (Feb.) 1937.

7. Stoeckel, K. H.: Ueber einen Fall von intrathorakaler Entodermcyste im Mediastinum posterius bei einem Neugeborenen, Zentralbl. f. Gynäk. **59**:2178-2183, 1935.

moid cysts, teratomas and enlarged glands, must be ruled out before a cyst of the type described can be correctly diagnosed. It seems an impossibility always to differentiate such mediastinal masses preoperatively by means of present day knowledge and laboratory methods.

PROGNOSIS

Some of the cysts [4] are accidentally found at autopsy in adults who have had no symptoms. These produce no ill effects. However, in other instances [8] they enlarge sufficiently to produce pressure on the respiratory passages. Case reports indicate that when once the cysts become large enough to produce symptoms there is always a steady progression of these symptoms until operative intervention is attempted or until death results. Although the symptoms may be intermittent, as in the case reported here, a fatal outcome seems inevitable unless some operative intervention is successful.

TREATMENT

Since the condition of these patients in every instance becomes steadily worse once the symptoms of pressure on the respiratory passages begin, it is imperative that some type of surgical intervention be attempted. Brown [9] successfully aspirated a mediastinal cyst of unknown type in a 35 year old woman, who had complete disappearance of symptoms. No follow-up observation of this case was reported, and it is questionable how long such a cyst would remain decompressed. The cells lining the cyst would be expected to continue secreting unless they were destroyed in some way. Walzel,[10] in 1933, successfully removed one of these cysts from a 25 year old man, who was completely relieved of symptoms. In view of the improving technic and rapidly decreasing mortality in surgery of the chest, there is reason to believe that many patients will in the future be completely cured by early recognition and complete removal of these benign cysts.

8. Fletcher.[6a] Blackader and Evans.[6b]
9. Brown, L. G.: Mediastinal Cyst, Radiology **7**:436-438, 1926.
10. Walzel, P.: Lungentumoren, Beitr. z. klin. Chir. **158**:654-670, 1933.

RHABDOMYOSARCOMA OF THE PROSTATE

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Sarcoma of the prostate is uncommon. In an excellent review of the literature up to 1934, Lowsley and Kimball [1] stated that they could find only 132 reported cases in which the diagnosis had been verified by microscopic evidence; 20 additional cases have been reported since, bringing the total number of authentic cases to 152.

AGE

Persons of any age may be affected. The youngest patient with this condition was an infant of 4 months; and the oldest, a man of 88 years. However, the highest incidence is encountered during the first decade of life, in which occur approximately 25 per cent of all cases. After the tenth year the disease occurs much less frequently but shows no appreciable relation to age. It is noteworthy that prostatic sarcoma is relatively most frequent in early infancy, 11 cases having been reported in patients under 1 year of age.

PATHOLOGY

Many types of sarcoma of the prostate have been described. The most common is the round cell sarcoma, which accounts for 27 per cent of the reported cases. The next most common is the spindle cell variety, which comprises 22 per cent of the total. The remaining types include lymphosarcoma, fibrosarcoma, myxosarcoma, chondrosarcoma, angiosarcoma, giant cell sarcoma, mixed cell sarcoma, leiomyosarcoma and rhabdomyosarcoma.

Ewing [2] said, "The only well defined variety of prostatic sarcoma is the rhabdomyosarcoma." It was first described by Kaufmann,[3] in 1902,

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From the Department of Urology, Department of Pediatrics and Department of Pathology of the Jewish Hospital.

1. Lowsley, O. S., and Kimball, F. M.: Sarcoma of the Prostate, with a Review of the Literature, Brit. J. Urol. **6**:328 (Dec.) 1934.

2. Ewing, J.: Neoplastic Diseases, Philadelphia, W. B. Saunders Company, 1928, p. 831.

3. Kaufmann, E., in Socin, A., and Burckhardt, E.: Die Verletzungen und Krankheiten der Prostata, Stuttgart, Ferdinand Enke, 1902, p. 396.

and since then isolated case reports have appeared in the literature. A total of 11 instances of this type of tumor have been described, comprising 7 per cent of all the cases of sarcoma of the prostate.

Sarcoma of the prostate is a rapidly growing tumor, which usually attains considerable proportions; it may reach the size of a child's head, occupying the entire pelvis and the lower part of the abdomen. Rarely, however, it may be so small as to escape macroscopic detection. The surface of the tumor is usually smooth and regular. Its consistency is firm, but it ordinarily does not have the hard, nodular feel of a carcinoma; at times it may be soft, doughy or cystic.

Regional extension by continuity occurs in the vast majority of cases. The bladder, urethra, seminal vesicles and rectum are frequently infiltrated. There may be extension to the perineum, producing a tumor in that region which ultimately goes on to ulceration.

As a mechanical effect of the prostatic enlargement, obstruction is produced at the neck of the bladder and in the prostatic portion of the urethra. Cystitis and ascending pyelonephritis usually follow. Frequently pressure is exerted on one or both ureters, with resultant hydroureter and hydronephrosis. Compression of the rectum is almost always present. A large tumor exerts pressure on the iliac vessels and on the nerve trunks of the pelvis.

Systemic metastases are frequent, occurring in about 40 per cent of the cases. The lungs and bones are most often involved, but metastases have been found in practically every organ.

SYMPTOMATOLOGY

The outstanding symptoms are those due to urinary obstruction. Early in the disease, frequency of urination, urgency and dysuria occur; later, complete retention commonly ensues. Hematuria is not observed often. There may be fever due to pyelonephritis, which is a frequent complication. As a terminal event, uremia may supervene.

Compression of the rectum, which is present to some degree in practically every case, produces difficulty in defecation. When there is considerable encroachment on the rectal lumen, ribbon stools are observed. Rectal bleeding occurs when the tumor ulcerates into the wall of the rectum.

Edema of the legs and of the scrotum may develop as the result of pressure on the veins of the pelvis. Similarly, pains in the legs may be produced by pressure on nerve trunks.

When growth is advanced, the tumor may appear as a large abdominal mass arising from the pelvis or as a mass in the perineum. At this stage there is usually marked cachexia.

The disease runs a rapid course, with an invariably fatal termination, the average duration of life after the onset of symptoms being

about nine months. In children, however, the tumor is apparently more malignant than in adults. In patients up to the age of 10 years, three months is the average interval between the development of symptoms and death. Katzmann [4] reported the case of a child of 13 months who died nine days after symptoms were first noted.

DIAGNOSIS

The diagnosis of prostatic sarcoma has rarely been made before operation or autopsy. For adults the diagnosis is usually difficult, since the clinical picture may closely resemble that produced by benign hypertrophy, carcinoma, tuberculosis, abscess or cyst of the prostate.

For children, however, the diagnosis should not prove difficult if the possibility of the lesion is borne in mind. Urinary frequency, dysuria or acute retention of urine, with or without accompanying difficulty in defecation, is a symptom which calls for prompt examination of the prostate by rectal palpation. A tumefaction of that gland in a child is almost always due to sarcoma; the prostate is usually smooth, regular and firm. Excretory urography is of distinct diagnostic value; in infants, in whom intravenous injection may be difficult, the urographic medium may be injected subcutaneously, as described by Beer and Theodore.[5] By means of the urogram there can be demonstrated elevation of the floor of the bladder due to the enlargement of the prostate and filling defects of the bladder if that organ is infiltrated by the tumor. One may also see displacement or compression of the ureters and evidence of hydroureter and hydronephrosis. Often cystoscopy cannot be performed because the obstruction of the prostatic portion of the urethra and of the vesical neck will commonly prevent passage of the cystoscope. If visualization of the interior of the bladder is possible, there may be seen a greatly enlarged prostate and, frequently, malignant invasion of the bladder as well. In Ferguson's [6] hands biopsy by aspiration has been successfully employed in the diagnosis of carcinoma of the prostate; while there is no record of its use in the diagnosis of prostatic sarcoma, it should be of great assistance in such a case. By the technic of Ferguson an aspirating needle attached to a syringe is introduced into the prostate through the perineum, with a finger in the rectum as a guide to proper placement of the needle. This simple and innocuous procedure may spare the patient an exploratory exposure of the gland by suprapubic cystotomy or by perineal

4. Katzmann, K.: Beitrag zur Kenntnis von malignen Rhabdomyomen der kindlichen Prostata, Frankfurt. Ztschr. f. Path. **41**:297, 1931.

5. Beer, E., and Theodore, F. H.: Excretory Urography After Subcutaneous Injection of Neoskiodan, J. A. M. A. **103**:181 (July 21) 1934.

6. Ferguson, R. S.: Prostatic Neoplasms: Their Diagnosis by Needle Puncture and Aspiration, Am. J. Surg. **9**:507 (Sept.) 1930.

section. Roentgenograms of the chest and of the bones may prove helpful in establishing a diagnosis, since metastases to the lungs and bones occur frequently.

Sarcoma of the prostate in the child has most commonly been confused with prostatic abscess. This is because the sarcomatous prostate is at times soft and doughy. The presence of fever, which is the result of the renal infection so frequently associated with prostatic sarcoma, further misleads the physician into believing that an abscess of the prostate is present. On the basis of such an erroneous diagnosis, in a number of cases reported in the literature the prostate has been incised by way of the perineum, a procedure followed shortly by extensive sarcomatous implantation of the operative wound. Prostatic sarcoma in children must also be differentiated from cyst of the prostate or of the seminal vesicle. The consistency of the cyst is characteristic; in doubtful cases an aspirating needle introduced through the perineum will result in the evacuation and collapse of the cyst. If there is widespread invasion of the pelvis, sarcoma of the prostate may be confused occasionally with retroperitoneal sarcoma, but in such cases it can usually be determined by rectal examination that the tumor arises from the prostate.

TREATMENT

Thus far all methods of treatment have met with failure. Since the capsule of the prostate is already extensively involved by the time symptoms make their appearance, prostatectomy, whether performed by the suprapubic route or by the radical perineal operation, does not effect a cure. Operative procedures should be limited to palliation of symptoms. The usual requirement is drainage of the bladder, which is best accomplished by suprapubic cystostomy. Radium and roentgen therapy have succeeded in prolonging life; they appear to be the treatment of choice. Bumpus [7] reported the following results in a series of 5 cases so treated: A man of 59 years was kept alive seven and one half years, a man of 69 lived three years, a man of 64 was still alive two years after treatment was instituted and for a man of 28 years and a child of 3 years the treatment was a complete failure.

In the accompanying table are listed the authentic cases of rhabdomyosarcoma of the prostate which have been found reported in the literature.

The following case is the twelfth recorded instance of rhabdomyosarcoma of the prostate.

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7. Bumpus, H. C., Jr.: Radium and Roentgen Ray in the Treatment of Sarcoma of the Prostate, J. Urol. **14**:519 (Nov.) 1925.

REPORT OF A CASE

A boy 2½ years old was seen in consultation by two of us (P. K. and H. C.) on March 4, 1937. Seven weeks previously the child's mother noted the onset of urinary frequency, urgency and painful micturition. These symptoms became progressively more marked, particularly during the two weeks before consultation, and at the time of examination the patient urinated or attempted to do so every ten minutes. Urination was accompanied by intense pain; the urine was voided in

Summary of Reported Cases of Rhabdomyosarcoma of the Prostate

Case Number	Year	Author	Age	Duration After Initial Symptoms	Regional Extension	Metastases
1	1902	Kaufmann [3]	9 mo.	7 wk.	None	None
2	1902	Kaufmann [3]	4 yr.	5 mo.	Bladder, urethra, seminal vesicles	None
3	1902	Kaufmann [3]	26 yr.	4 mo.	Bladder, urethra	Liver, lungs, pleura, stomach, thyroid, dura, bones
4	1908	Greig, D. M.: Brit. J. Child. Dis. **5**: 185, 1908	4 yr.	3 mo.	Bladder	No autopsy
5	1916	Squier, J. B.: Surg., Gynec. & Obst. **23**: 341, (Sept.) 1916	40 yr.	?	Rectum	No autopsy
6	1926	Smith, R. R., and Torgerson, W. R.: Surg., Gynec. & Obst. **43**: 328 (Sept.) 1926	31 yr.	4 mo.	Bladder, urethra, rectum	Lungs, pleura, bones, regional lymph glands
7	1926	Kretschmer, H. L.: J. Urol. **16**: 301 (Oct.) 1926	31 yr.	?	?	No autopsy
8	1931	Katzmann [4]	13 mo.	9 da.	None	None
9	1931	de Rom, F., and Thomas, M.: Ann. et bull. Soc. roy. de méd. de Gand **10**: 144 (Nov.-Dec.) 1931	23 yr.	4 mo.	Bladder, urethra, rectum, symphysis pubis	Iliac and lumbar nodes
10	1935	Foucar, F. H.: Am. J. Path. **11**: 753 (Sept.) 1935	26 yr.	6 wk.	Seminal vesicles, rectum	Thyroid, lungs, liver, bones and cervical, bronchial and hilar lymph nodes
11	1936	Lahayville and Diss: Arch. d. mal. d. reins **10**: 181 (March) 1936	36 yr.	3 mo.	Bladder	No autopsy

small amounts, often only a few drops at a time. Gross hematuria had never occurred. During the preceding week the stools were flattened and ribbon-like.

The child was delivered at term with high forceps, with resultant intracranial injury, and since birth there had been evidence of rather pronounced mental retardation. He had bronchopneumonia at the age of 18 months; tonsillectomy was performed at 22 months.

On examination the child presented the coarse features and facies associated with retarded mental development. There was a ridge at the site of the sagittal suture of the skull, produced by the sharp angulation of the frontal bones. The eyes, ears, nose, mouth and throat showed no abnormal findings. The neck, heart and lungs were normal. The bladder was distended, reaching to the level of the umbilicus. No other abdominal viscera or masses were palpable. The external genitalia were normal. There was slight edema of both lower extremities, more

noticeable on the left. The reflexes were normal. On rectal palpation a large, smooth, hard, globular mass was felt bulging into the anterior wall of the rectum to such a degree as almost to obliterate its lumen. The mass occupied most of the pelvic cavity but was somewhat more extensive on the right; it gave the impression of arising from the region of the prostate. The rectal wall itself was intact.

The urine was grossly clear. The reaction was acid; the specific gravity was 1.016; there were a faint trace of albumin and no dextrose; the sediment contained many hyaline casts and an occasional leukocyte, but a smear showed no bacteria.

The temperature, pulse and respiration were normal. A roentgenogram of the chest showed no abnormal findings. Catheterization was attempted, but an impassable obstruction was encountered in the posterior portion of the urethra.

A roentgenogram of the urinary tract revealed that the left kidney was of normal size and the right, enlarged; there was no evidence of urinary calculus. Excretory urography was performed with subcutaneous administration of 100 cc. of a 7 per cent solution of diodrast. The right kidney functioned poorly, as was indicated by delayed excretion and faint concentration of the urographic medium; its calices and pelvis were considerably dilated; the corresponding ureter was widened throughout its entire extent. The left kidney functioned well, and its calices and pelvis were normal in configuration. The left ureter was of normal caliber, but in the lower two thirds of its course it was markedly displaced to the left. The bladder was distended and displaced upward; its left lateral wall appeared flattened. The floor of the bladder was elevated and presented finger-like filling defects which were most pronounced on the right (fig. 1).

A diagnosis of sarcoma of the prostate was made. The hydroureter and hydronephrosis on the right and the displacement of the left ureter were interpreted as secondary effects of the pressure from the tremendously enlarged prostate. Hospitalization was advised, and the patient entered the Jewish Hospital on March 5.

On his admission to the hospital the physical findings were essentially as previously described. The temperature was 100 F., the pulse rate 100 and the respiratory rate 24 per minute. The erythrocyte count was 4,150,000 per cubic millimeter; the hemoglobin value was 88 per cent. The leukocyte count was 11,500 per cubic millimeter, with 76 per cent polymorphonuclear neutrophils and 24 per cent lymphocytes. The Kline test of the blood gave a negative reaction. Chemical examination of the blood showed nonprotein nitrogen, 19 mg.; total nitrogen, 1,026 mg., and sugar, 72 mg. per hundred cubic centimeters, with albumin, 3.76 per cent; globulin, 2.54 per cent, and the albumin-globulin ratio, 1.48.

A study made with a barium sulfate enema revealed marked compression and displacement of the rectum and sigmoid flexure by a large extracolonic mass. The lumens of both the rectum and the sigmoid flexure were almost completely obliterated; the rectum was displaced to the left, and the sigmoid flexure was pushed to the left and upward (fig. 2). Attempts were made to introduce a catheter into the bladder with the aid of filiform guides, but without success, all instruments becoming obstructed in the posterior portion of the urethra. Although the bladder remained distended, urination occurred by overflow. Owing to the large size of the tumor and its extensive encroachment on the rectum, sigmoid flexure, bladder and ureters, the condition was considered inoperable. The patient was discharged from the hospital five days after admission, and roentgen therapy was commenced.

Two days later vomiting developed, and the temperature rose to 104 F. The child was therefore readmitted to the hospital on March 12. His general condition was poor. On rectal palpation the tumor seemed to have grown larger. The temperature remained elevated, vomiting continued and the patient became extremely weak. He declined rapidly and died on March 16, nine weeks after the onset of symptoms.

Autopsy was performed by one of us (M. M. S.).

Macroscopic Description.—The body was well developed. The skin was pale, the superficial lymph nodes were not enlarged and there was dependent edema

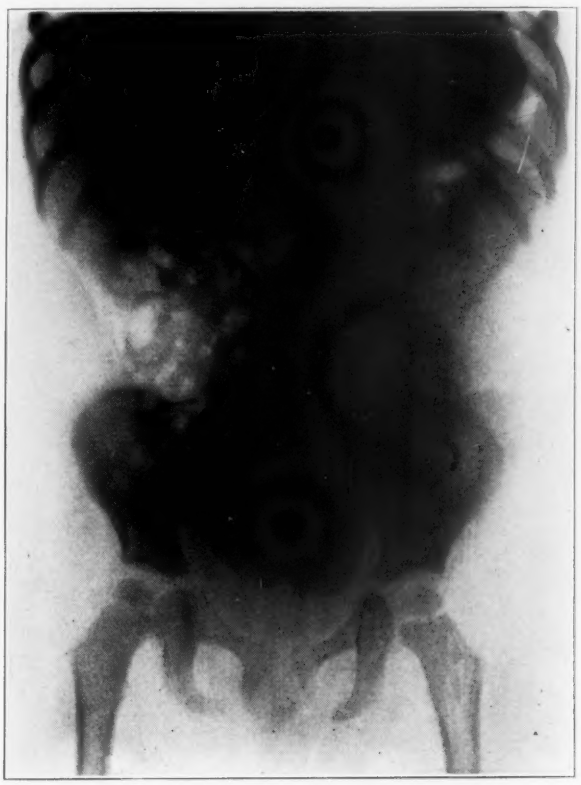

Fig. 1.—Excretory urogram.

of the lower extremities. There was nothing unusual about the head, neck or chest. The abdomen was protuberant. The peritoneal cavity contained about 10 cc. of pale yellow fluid; the peritoneal surfaces were smooth and glistening. The bladder was markedly distended and reached the level of the umbilicus. There was 100 cc. of pale yellow fluid in the right pleural cavity and no fluid in the left; the pleural surfaces were smooth and glistening. The pericardial cavity was not unusual in appearance.

The right kidney measured 8.5 by 5 by 3 cm. and weighed 110 Gm. The capsule was thick and stripped with difficulty, leaving a pale red, irregular

surface with multiple discrete and confluent depressed gray areas measuring up to 1 by 0.5 cm. Some of these were filled with a creamy yellow material. Similar gray areas, with surrounding red discolorations, were noted on both aspects of the renal capsule. On section of the kidney, the cut edges bulged; the cortex and medulla were not well demarcated. In places the cortex measured 0.4 cm. and the medulla 1.5 cm. in the axis of a pyramid. There were numerous gray-white areas on the surface of the kidney measuring up to 1 by 1 cm. In these the normal landmarks were not apparent. The calices and renal pelvis were dilated and filled with gray granular material; the mucosal surface was granular.

Fig. 2.—Roentgen study made with a barium sulfate enema.

reddened and covered with a gray film. The right ureter was dilated, its wall was thickened and the mucosal surface was granular. The left kidney measured 8 by 3.5 by 2.5 cm. and weighed 70 Gm. The capsule stripped readily, leaving a smooth, pale red surface with prominent fetal lobulations. On the cut surface the cortex and medulla were well demarcated; the cortex measured 0.6 cm. and the medulla 1.6 cm. in the axis of a pyramid. The calices, renal pelvis and corresponding ureter were somewhat dilated; the mucosal surface was smooth and in places revealed minute red areas (fig. 3).

There was a roughly oval, well circumscribed, firm mass in the region of the prostate, which measured 9 by 6 by 3 cm. This mass practically filled the pelvic cavity, displacing the rectum to the left and extending upward over the posterior wall of the bladder beyond the level at which the ureters entered the bladder. The external surface was covered with pink and gray membranous tissue. The sectioned surfaces were composed of pearly gray, glistening tissue, with irregular areas of

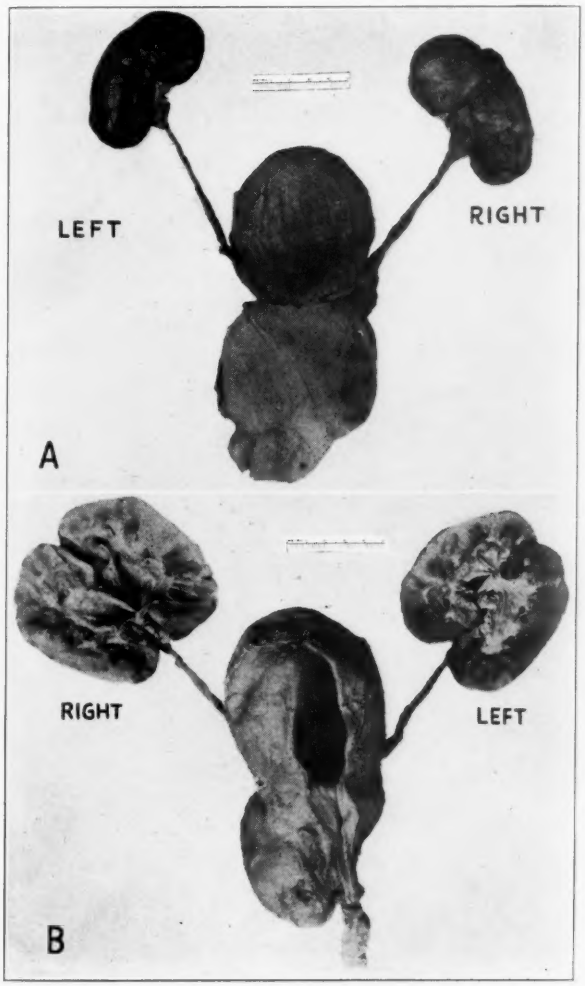

Fig. 3.—*A*, posterior view, showing sectioned surfaces of the tumor of the prostate. Note the marked distention of the urinary bladder and the numerous cortical abscesses of the right kidney. *B*, anterior view, showing the distention of the urinary bladder, the thickness of the vesical wall and the compression of the prostatic urethra by the tumor of the prostate. In the sectioned surfaces of the right kidney, note the obliteration of the normal landmarks by the discrete and confluent abscesses. The calices and renal pelvis are dilated, and their mucosal surface is granular.

pale yellow and red tissue. In one region there was a network of thin gray strands, with intervening red and white tissue. The seminal vesicles were not apparent (fig. 3 *A*).

The bladder measured 17 by 8 by 6 cm.; it contained cloudy yellow urine. The wall was 0.3 cm. thick; the mucosal surface was finely granular and revealed discrete and confluent red areas. In the region of the trigon the bladder was

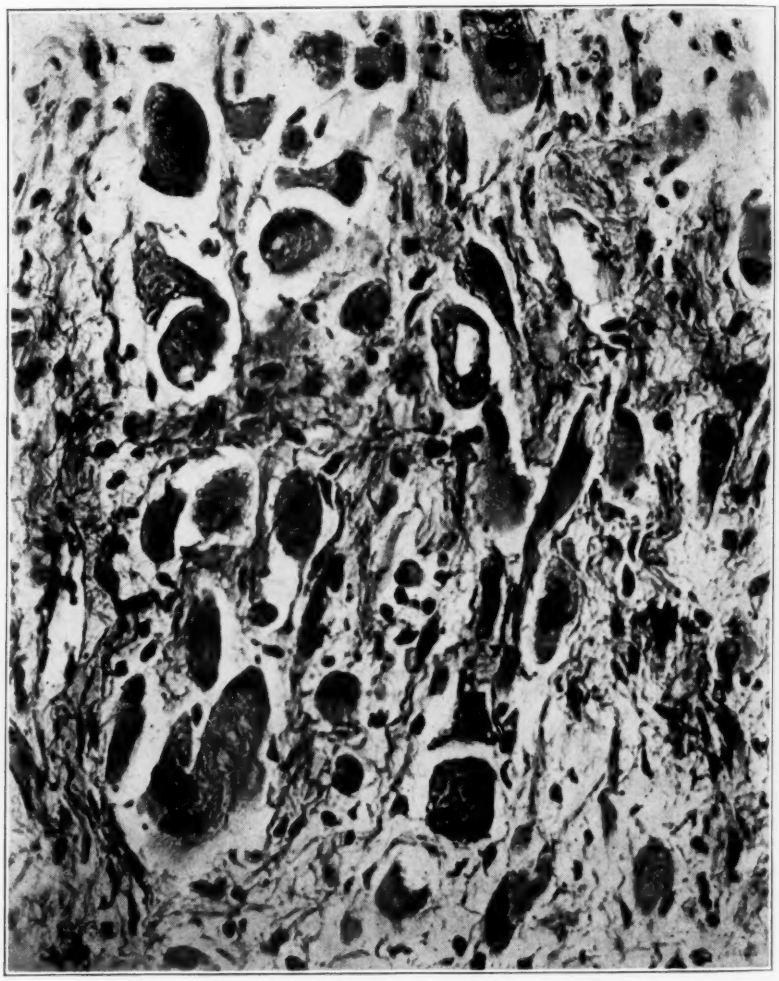

Fig. 4.—Photomicrograph of a section made through the tumor, showing marked variation in cellular structure. Note the gradation from small spindle-shaped cells to large, bizarrely shaped, multinucleated giant cells containing irregular nuclear masses. Hematoxylin and eosin stain; × 700.

infiltrated by pearly gray, glistening tissue, resembling that of the tumor of the prostate. The ureteral orifices were patent. The right ureter was compressed between the tumor and the vesical wall and was bound down by strands of gray

membranous tissue. The prostatic portion of the urethra was compressed by the lateral lobes of the prostate. The walls of the urethra were infiltrated with tissue similar to that of the tumor, but no areas of ulceration were noted. There were no obstructions within the membranous or anterior portion of the urethra (fig. 3*B*).

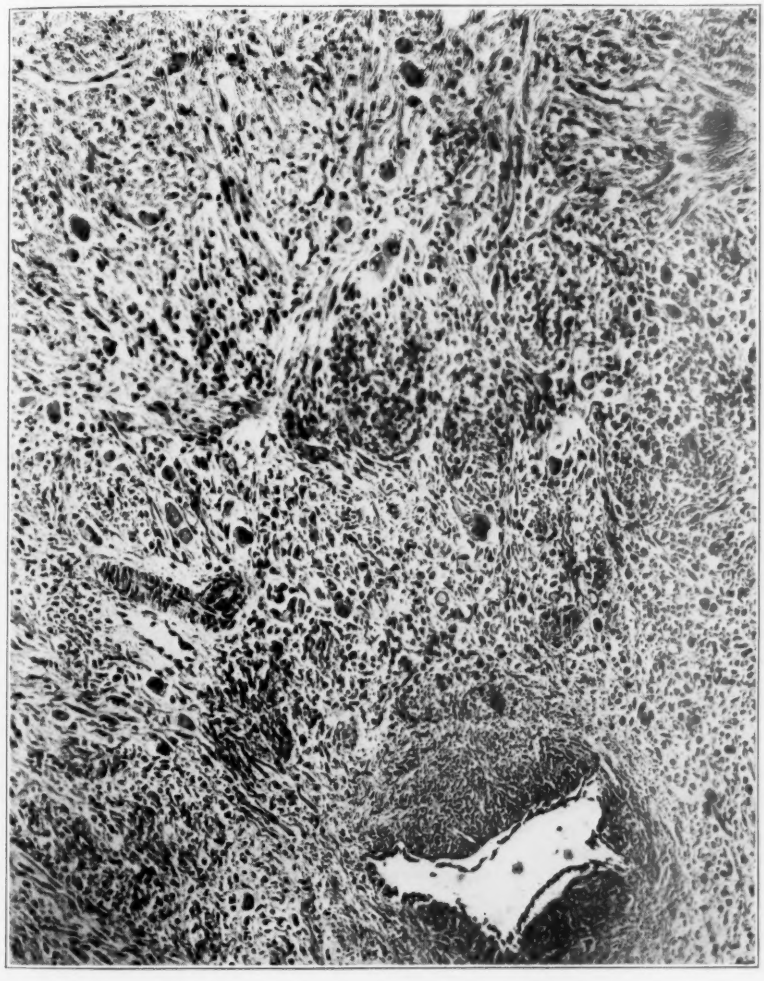

Fig. 5.—Photomicrograph of a section made through the tumor, showing a normal acinus with a surrounding broad layer of connective tissue. Note the adjacent tumor cells arranged in irregular bundles. Hematoxylin and eosin stain; × 150.

The lumen of the rectum was markedly narrowed; the mucosal surface was smooth and pale red; the wall was not of unusual appearance. There was no evidence of neoplastic infiltration.

The remaining organs showed nothing unusual. There were no systemic metastases.

Microscopic Description.—In the preparation from the right kidney the cortical surface was covered by a broad layer of polymorphonuclear leukocytes contained within pink-staining granular débris. In one area this layer was continuous with an accumulation of similar cells which replaced a large portion of the renal parenchyma. Similar foci throughout the kidney contained clumps of lavender-staining material. The glomeruli were unevenly distributed, the glomerular capillaries were distended with red blood cells, the subcapsular spaces were narrow and Bowman's capsules were delicate. Some glomeruli were markedly distended

Fig. 6.—Photomicrograph of a section, showing broad striations within elongated tumor cells. Phosphotungstic acid stain; × 1,000.

with polymorphonuclear leukocytes; in these the subcapsular spaces were obliterated. In most areas the tubular structures were poorly preserved, and the lining cells were desquamated. Some tubules were markedly distended with polymorphonuclear leukocytes. The interstitial connective tissue was spread apart by small round cells, large mononuclear cells and polymorphonuclear leukocytes. The vascular channels were distended with red blood cells, and in places areas of extravasated red cells were noted. In a preparation from the left kidney, the cyto-architecture was well preserved.

Preparations from the tumor which were stained with hematoxylin and eosin revealed marked variation in the size, shape and staining characteristics of the cellular elements. Broad, elongated, spindle-shaped cells resembling muscle fibers were arranged into bundles in a whorl-like formation or were spread within delicate connective tissue. The nuclei were oval and elongated, with dense chromatin material and thick nuclear membranes. Many nuclei were pyknotic, hyperchromatic and unevenly stained. No mitotic figures were noted. Bizarrely shaped, multinucleated giant cells were noted throughout the tumor; the nuclei varied from 1 to 3 and were irregularly distributed within the cells. In some of these cells the nuclei were fused into dense masses. The cytoplasm was abundant, unevenly stained and vacuolated. Elsewhere, groups of small spindle-shaped cells were compactly arranged about distended blood vessels in concentric or palisade formation. The nuclei were dense and pyknotic, varying from oval to round, with a sparse amount of uniformly pale-staining cytoplasm (fig. 4). Acinar structures were few, widely separated and surrounded by a dense layer of connective tissue. The lining cells were composed of one or more layers of uniform cuboidal cells, which showed no evidence of neoplastic change; the lumens were clear (fig. 5). The stroma was loose or appeared as dense bands of connective tissue harboring tumor cells and broad nerve bundles. In some areas in this region the tumor tissue contained many blood vessels; these channels were distended with red blood cells or with a network of fibrin containing polymorphonuclear leukocytes, small round cells, mononuclear cells and granular débris. Occasional areas of necrosis were noted.

In preparations stained by the Van Gieson method, the tumor cells were pale yellow and were separated by loose or dense pink-staining connective tissue.

In preparations stained with phosphotungstic acid, many elongated tumor cells and multinucleated giant cells contained cross striations. These were delicate and close together in some cells and thick and spread apart in others. Within the latter the striations appeared spiral in arrangement (fig. 6).

Examination of numerous preparations showed no evidence of structure typical of the seminal vesicles.

Preparations from the remaining organs showed nothing unusual. There were no metastases.

Anatomic Diagnosis.—The diagnosis was rhabdomyosarcoma of the prostate, with extension into the bladder, urethra and seminal vesicles; compression of the prostatic urethra and of the rectum; distention of the bladder; perinephritis and pyelonephritis (right), and hydrothroax (right).

COMMENT

The prostate is a partly muscular and partly glandular organ which surrounds the first portion of the urethra of the male. Histologically, it is composed of a conglomerate of small, compound, tubuloalveolar glands. These give rise to excretory ducts which open into the urethra on the right and on the left of the verumontanum (colliculus). The glands vary in size; there is no distinct basement membrane; the epithelium rests on a layer of connective tissue with dense, elastic networks and numerous blood capillaries. The lining cells are low cuboidal and in places simple or pseudostratified columnar cells. The interstitial tissue is abundant; it consists of dense connective tissue, with collagenous

fibers and elastic networks, and of abundant smooth muscle fibers arranged in strands of various thickness. The connective tissue forms a capsule at the periphery of the organ. Together with smooth muscle it is arranged in thick broad septums, widely separating the glands from

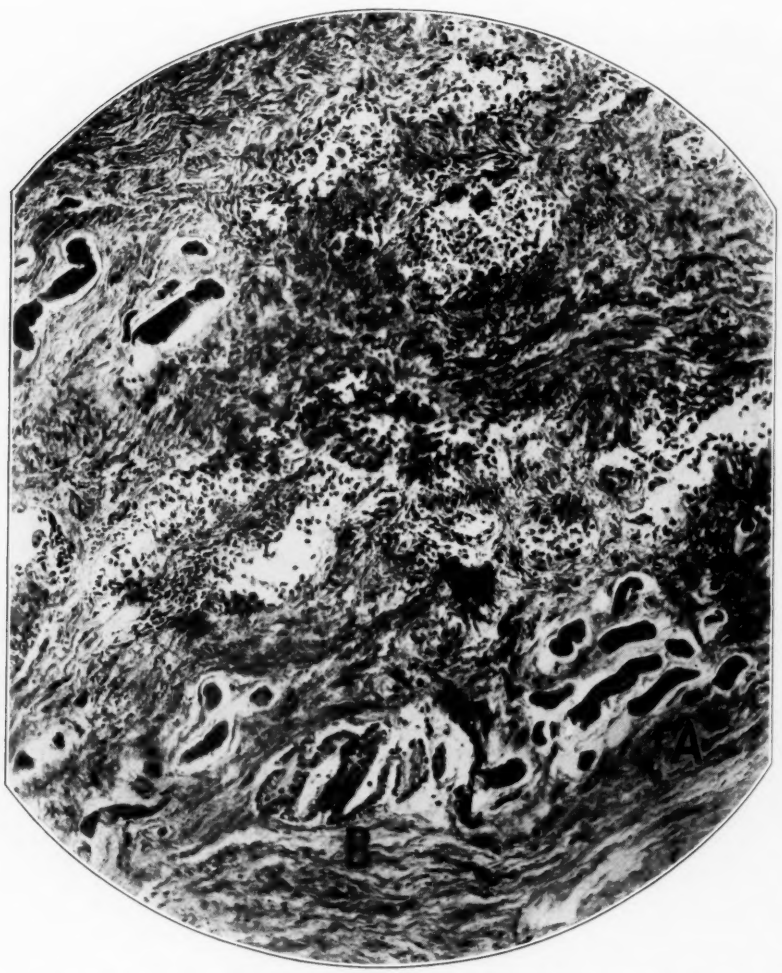

Fig. 7.—Photomicrograph of a section from a normal prostate, showing striated muscle fibers within the stroma and adjacent surrounding acinar structures. *A* indicates group of striated muscle fibers; *B*, group of normal prostatic acini. Hematoxylin and eosin stain; × 600.

each other and radiating from the region of the verumontanum to the periphery.

Although smooth muscle fibers make up the bulk of the musculature of the prostate, the gland also contains a small amount of striated muscle.

To quote Spalteholz,[8] "It [the prostate] consists in the largest part of glandular substance which as corpus glandulare surrounds the first portion of the urethra in the form of a broad clasp, open in front. This clasp is closed to form a ring by means of muscular tissue, the m. prostaticus. The latter consists, in its upper part, of smooth muscle fibers and is connected with the m. sphincter vesicae; in the lower part it is formed of striped fibers and is inseparably continuous with the m. sphincter urethrae membranaceae. The muscle fibers run especially transversely and radiate out into the glandular substance and upon its surface." Sobotta and McMurrich[9] stated: "The prostatic musculature is chiefly involuntary in character, but at the lower extremity of the organ it becomes intermingled with the striated fibers of the sphincter urethrae membranaceae." In serial sections as well as in the ordinary sections of the normal prostate, we have been able to demonstrate striated muscle fibers within the gland (fig. 7).

Rhabdomyosarcoma of the prostate has been explained by most writers as a new growth arising from a congenital rest within the gland. Others have assumed a change from smooth to striated muscle in the neoplastic transformation of this type of tumor. However, the occurrence of striated muscle in the normal prostate makes it unnecessary to assume the modes of origin just cited, since these muscle fibers can themselves give rise to the tumor.

SUMMARY

The clinical features of sarcoma of the prostate are summarized.

A case of rhabdomyosarcoma of the prostate, the twelfth on record, is reported.

The origin of rhabdomyosarcoma of the prostate from striated muscle fibers which are normally present in the gland is suggested.

855 Ocean Avenue.
1025 East Sixteenth Street.
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8. Spalteholz, W.: Hand Atlas of Human Anatomy, Philadelphia, J. B. Lippincott Company, 1903, vol. 3, p. 592.

9. Sobotta, J., and McMurrich, J. P.: Atlas and Text-Book of Human Anatomy, Philadelphia, W. B. Saunders Company, 1906, vol. 2, p. 136.

PANCREATIC STEATORRHEA

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AND
F. W. SCHLUTZ, M.D.
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Two years ago Parmelee [1] reviewed briefly the literature on pancreatic steatorrhea and presented 2 cases of his own. Including his cases, we have been able to find 10 reported cases. It seems entirely possible, however, that in some cases the condition has been incorrectly diagnosed as celiac disease and for that reason the cases have never been reported in the literature or have been reported under a false diagnosis.

The earliest report of pancreatic steatorrhea was made by Garrod and Hurtley [2] in 1913. They reported the cases of 2 brothers, only 1 of whom it was their good fortune to observe. The other had died earlier with symptoms suggestive of the disorder noted in the one whom they observed. The latter was in perfect health except for the passage of numerous large, pale yellow, foul-smelling stools containing obvious undigested fat. He apparently digested carbohydrate well, but when given a diet with high fat content he passed stools containing 60 per cent of the total fat as neutral fat.

Miller and Perkins [3] reported a typical case; analysis showed 52 per cent fat in the dried stool. The proportion of neutral fat, however, was increased only slightly above the level observed in celiac disease. The child died at home of septic pneumonia following the extraction of a tooth, a general anesthetic having been used. Permission for autopsy was not obtained.

Clarke and Hadfield,[4] in 1924, reported a typical case in a 4 year old child with infantilism who died of bronchopneumonia. Autopsy

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From the Department of Pediatrics, University of Chicago.

Read at the meeting of the American Academy of Pediatrics (Region III), Chicago, Oct. 15, 1937.

1. Parmelee, A. H.: The Pathology of Steatorrhea, Am. J. Dis. Child. **50**: 1418 (Dec.) 1935.

2. Garrod, A. E., and Hurtley, W. H.: Congenital Family Steatorrhea, Quart. J. Med. **6**:242, 1912-1913.

3. Miller, R., and Perkins, H.: Congenital Steatorrhea, Quart. J. Med. **14**:1, 1920.

4. Clarke, C., and Hadfield, G.: Congenital Pancreatic Disease with Infantilism, Quart. J. Med. **17**:358, 1923-1924.

revealed miliary abscesses of the lungs, bronchopneumonia, atrophy and fibrosis of the pancreas, the remaining portion being estimated at one-twentieth of the normal organ, and fatty change in the liver.

Harper,[5] in 1930, reported 2 cases in both of which analysis of the stools gave characteristic findings and in 1 of which typical alterations were observed at autopsy (bronchopneumonia, fatty change of the liver and pancreatic fibrosis). Both of her patients died of bronchopneumonia. She divided pancreatic steatorrhea into four types: congenital, with infantilism; congenital, without infantilism; acquired, and those occurring at puberty.

Siwe [6] reported 1 case, in 1932, in which the stools and observations made at autopsy were typical.

Hess and Saphir,[7] in 1935, reported 3 cases, characteristic postmortem observations being made in each. All 3 patients died of bronchopneumonia, and fibrosis was observed in the pancreas of each.

Parmelee's [1] 2 patients died of bronchopneumonia. Autopsy was performed on only 1 of these, and the changes were characteristic. Analysis of the stools for fat was not reported.

Of these 10 cases, analysis of the stools for fat is reported in 5 and autopsy in 7.

Because of the rarity of pancreatic steatorrhea and because we were fortunate enough to be able to investigate the clinical and laboratory aspects in greater detail than is usually possible and to describe the results of a postmortem examination, the following case is reported:

REPORT OF A CASE

A boy, the third of the 4 children of a farmer, had a reputedly normal birth and early development and was apparently well until the age of 1½ years. At this time he contracted severe bronchitis, which lasted about three weeks. After this he had bouts of coughing every two or three weeks which lasted three or four days each. These spells of coughing became more frequent and were of greater duration as the boy grew older, and during the year before we saw him were almost constant. He raised small amounts of thick yellow material, most of which was swallowed. His cough was worse when he arose in the morning and was more frequent and more severe during the day than at night. His breath was frequently offensive. He had had these symptoms for three and a half years.

During the two years preceding admission to the Bobs Roberts Memorial Hospital, the boy was said to have passed large, pale yellow, foul-smelling stools which

5. Harper, M.: Two Cases of Congenital Pancreatic Steatorrhea with Infantilism, M. J. Australia **2**:663, 1930.

6. Siwe, S.: Total Agenesis of the Exocrine Portion of the Pancreas, Deutsches Arch. f. klin. Med. **173**:339, 1932.

7. Hess, J., and Saphir, O.: Celiac Disease (Chronic Intestinal Ingestion): A Report of Three Cases with Autopsy Findings, J. Pediat. **6**:1, 1935.

contained visible undigested fat. That this symptom may have been of greater duration is perfectly possible, in view of the fact that the parents paid little attention to the boy's stools, as compared with observation of his pulmonary symptoms. The boy had three or four movements daily and suffered frequent nocturnal incontinence of feces. There was never any blood in the stools.

In spite of a superb appetite (five or six meals daily), the boy gained weight poorly if at all; he weighed only 30 pounds (13.6 Kg.) at the time of his death, although he was 5 years and 3 months of age. He weighed 24 pounds (10.9 Kg.) at the age of 2 years, 31 (14.1 Kg.) at 3 and at 4, and 33 (15 Kg.) at 5. A snap-

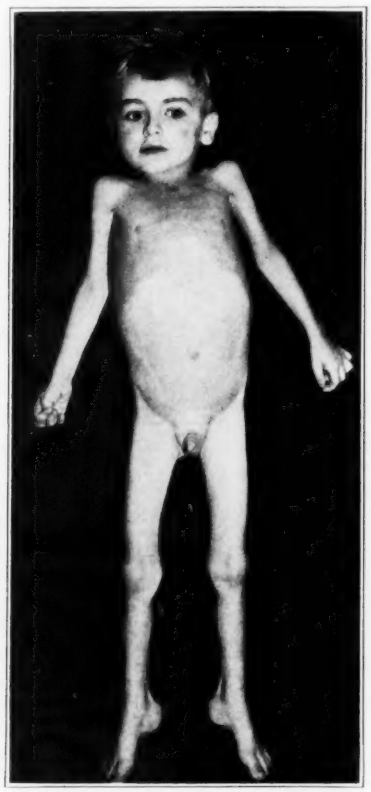

Fig. 1.—Full length view of the patient, showing emaciation with sparing of the face.

shot taken at the age of 3 years, just before the onset of intestinal disturbance, showed an apparently normal boy. He was seen by three physicians before his first visit to our clinic. All had obtained negative reactions to tuberculin tests. None had offered a diagnosis to the family. One of the physicians took roentgenograms which were said to show infection of the lungs and an enlarged liver and intestine. One physician apparently thought that the fecal symptoms were evidence of celiac disease, for the boy was given a diet high in protein. He gained weight with this diet, whereas he had lost weight with a mixed diet.

The family history was irrelevant.

Physical examination on his admission to the hospital showed a sad-eyed, poorly nourished boy of 5 years whose face alone was spared in the process of emaciation. He was barrel-chested and pot-bellied and exhibited clubbing of the fingers and toes. There were dark circles under the eyes, the lashes were long and silky and there was a peculiar bright flush of the cheeks. The lips were cyanotic. The tonsils were large and red. The lungs throughout were hyperresonant to percussion, the breath sounds were amphoric and numerous moist rales were heard over all parts of both lungs. The abdomen was protruding and tympanitic. The liver was palpable 4 cm. below the costal margin. The patient was slightly orthopneic and dyspneic and coughed frequently, raising little sputum and swallowing most of that.

The boy was in the hospital about four weeks before he died. Postural drainage was carried out daily, with poor success. Chronic maxillary sinusitis was discovered and was treated by irrigation. Roentgen examination disclosed scattered areas of infiltration throughout both lungs. The lesions were thought by the radiologists to resemble those of tuberculosis. The tuberculin test gave negative results.

Bronchoscopy was performed twice, with aspiration of large amounts of blood-tinged purulent material on both occasions. Culture of the material aspirated at the second bronchoscopy revealed an almost pure culture of beta hemolytic streptococci. Staphylococcus aureus was present (a few organisms being seen), but there were no spirochetes. Culture of blood taken at this time produced no bacterial growth.

When the large, pale yellow, foul-smelling stools, which were passed three or four times daily, were first observed, it was thought that the patient was suffering from celiac disease. A diet high in protein was instituted, with the addition of numerous bananas. With this diet the boy gained 1 pound (454 Gm.) in eighteen days. Meantime the stool was being analyzed to determine the total amount and the nature of the fat content. A small amount or absence of free fatty acid would indicate pancreatic steatorrhea, while a large amount of free fatty acid would be expected in true celiac disease. The results of this analysis, which caused us to change our diagnosis from celiac disease to pancreatic steatorrhea, were as follows (one stool, weighing 182 Gm., was analyzed): [8]

Contents of Stool	Percentages
Moisture	71
Fat in dry stool, total	42
Free fatty acid	None
Neutral fat	56
Nonsaponifiable fat	30
Fatty acids as soaps	14

In view of these findings we felt that the administration of pancreatic extract was needed to supply the lacking pancreatic lipase. Pancreatin in enteric coated pills was given daily during the remaining four days of life, in addition to the high protein diet. The boy had gained only slightly with the protein diet alone, but he gained two thirds of a pound (300 Gm.) on the first day that pancreatin was added. Unfortunately the pulmonary symptoms became so severe that he was

8. Howard A. Trangsrud (Jessie Horton Koessler fellow in surgery) performed this analysis.

never weighed again. He obviously succumbed to bronchopneumonia superimposed on the preexisting bronchiectasis. During the last ten days of life he had a gradually rising fever, increased cyanosis, cough and weakness. Respirations became increasingly shallow and labored, and he was kept in an oxygen tent during the last four days of life. His appetite, formerly excellent, failed during the febrile period which preceded death.

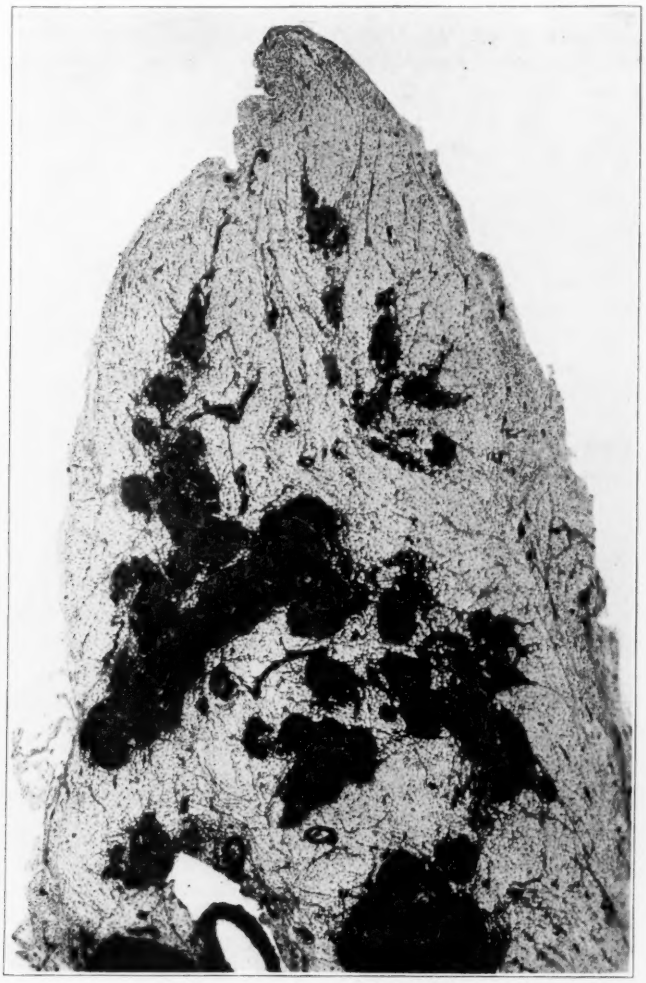

Fig. 2.—Low power photomicrograph of the pancreas, showing marked atrophy of acinar tissue, with replacement of the lost tissue by fat and fibrous tissue.

Six days before the boy died, a peculiar condition, vesicular glossitis, developed which was apparently unrelated to the rest of the clinical picture. This persisted until death.

Laboratory tests showed a normal blood count and normal urine. The Wassermann and Kahn tests gave negative reactions. The tuberculin test gave

a negative reaction. The serum calcium content was 9.8 mg. per hundred cubic centimeters. A test with phenolsulfonphthalein showed normal renal function. Culture of the stool showed the presence of Proteus vulgaris and Bacillus coli. The blood sugar curve was normal. Culture of the blood was sterile; culture of material taken at bronchoscopy showed beta hemolytic streptococci and Staph. aureus but no spirochetes.

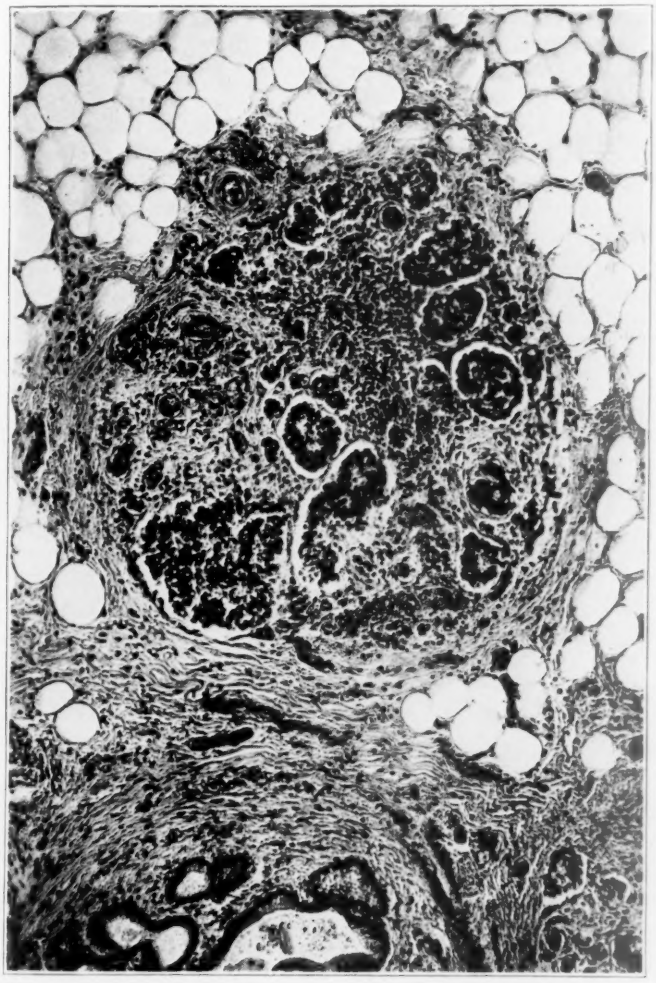

Fig. 3.—High power photomicrograph of the pancreas, showing great atrophy of acinar tissue and replacement by fibrous and fat tissue.

Reports of roentgen examinations were as follows: The first examination revealed clouding of the maxillary sinuses, an azygous pseudolobe of the lung and diffuse lesions throughout both pulmonary fields and hili, assumed to be tuberculous. The second examination revealed no evidence of rachitic change in the epiphyses of the long bones. There was a diffuse periosteal reaction in the tibia

and fibula associated with general osteoporosis—subperiosteal hemorrhage or cellular infiltration—as the result of anemia or leukemia. The lesions in the lungs possibly were indicative of leukemic infiltration. The third examination demonstarted the unchanged appearance of the lungs after bronchoscopy.

At autopsy both pleural cavities were partially obliterated by fibrous adhesions, and 100 cc. of yellow, fibrin-flecked fluid was present in the right pleural cavity. The tracheobronchial lymph nodes were all hyperplastic, one being as large as 3.5 by 4 by 2 cm. The right lung was mottled with purple areas of atelectasis and with nodular consolidations. The markedly dilated bronchi contained a mucopurulent exudate. There were small areas of fibrosis and consolidation about the bronchi. An azygous lobe was atelectatic and contained numerous miliary abscesses. The pathologic condition of the left lung resembled that of the right.

The liver was large, weighing 1,000 Gm. The cut surface was greasy. The hepatic duct was narrowed.

The pancreas was normally situated but was atrophic and markedly fibrosed. The cut surface showed the fibrosis better than the exterior; it revealed the presence of only a few normal-appearing acini. The pancreatic duct was not obstructed.

Microscopic examination of the pancreas revealed marked atrophy of at least 95 per cent of the acinar tissue, with replacement by fat tissue and fibrous tissue. The islets of Langerhans were unusually close together. The pancreatic ducts were seen in several places to be dilated and filled with a clear, homogeneous, pink-staining material. No calcification was seen in the ducts.

The liver on microscopic examination showed fatty infiltration throughout.

Microscopic sections of the lung revealed obvious bronchopneumonia and marked dilatation of the bronchi, with loss of the elastic tissue of the bronchial walls.

A small area of accessory pancreatic tissue was noted in the wall of the jejunum. Microscopically it showed changes similar to those seen in the pancreas.

COMMENT

It is our feeling that a careful total and differential analysis of the stool for fat should be carried out in all cases of steatorrhea as a means of differentiating between the pancreatic and the nonpancreatic type (celiac disease).

It is not possible to estimate the value of pancreatin therapy in our case, as its use was instituted so short a time before death. We have been unable to find any report speaking enthusiastically for its use in these cases. Until better therapeutic methods are devised, however, it seems justifiable to try various pancreatic extracts in the hope that their prolonged use in sufficient doses will prove beneficial.

Parmelee's observation that most victims of pancreatic steatorrhea die with bronchopneumonia is amplified by our case. Miliary pulmonary abscesses have also been observed previously in a few cases. The bronchiectasis in our case confuses the issue somewhat, as it is possible that there would have been terminal bronchopneumonia had the pancreatic steatorrhea not been present.

It is interesting to speculate on the possible correlation of the amount of pancreatic fibrosis with the percentage of neutral fat in the stool.

Our case is the only one of which we know in which there was complete lack of free fatty acid. The degree of pancreatic atrophy and fibrosis in our case was comparatively great. Whether the degree of atrophy and fibrosis can always be predicted on the basis of the amount of free fatty acid in the stool is a matter for future observation to decide.

NOTE.—Since this paper was submitted for publication, Margaret Harper [9] has published a report of 8 more cases.

9. Harper, M.: Congenital Steatorrhea Due to Pancreatic Defect, Arch. Dis. Childhood **13**:45 (March) 1938.

Progress in Pediatrics

CYSTIC FIBROSIS OF THE PANCREAS AND ITS RELATION TO CELIAC DISEASE

A CLINICAL AND PATHOLOGIC STUDY

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The pathology and pathologic physiology of celiac disease remain obscure in spite of the many attempts that have been made to understand them. It has become clearer in recent years that celiac disease is a clinical picture "characterized by arrest of growth, a distended abdomen, and attacks of diarrhoea with large, pale, foul-smelling stools" [1] rather than a disease entity and that the underlying pathologic condition may differ in different cases.[2] A tradition exists that pancreatic steatorrhea can be readily differentiated from idiopathic steatorrhea by the low percentage of split fat in the stools associated with the former and the normal percentage characterizing the latter. A careful survey of the literature, however, reveals few cases of either disease in which careful clinical observations have been followed by adequate postmortem examination. The present study was initiated because of the findings in case 44 (XX), in which a patient with celiac disease who had a high percentage of split fat in the stools and who had responded favorably to treatment for celiac disease was found at autopsy to have cystic fibrosis of the pancreas. This demonstrated that the recognized criteria of differentiation between the steatorrhea due to pancreatic insufficiency and that due to other causes are unreliable.

To establish more reliable criteria it is necessary to study cases in which normal acinar tissue has been proved by postmortem examination to be absent or inadequate and to compare them with cases of celiac disease associated with a normal pancreas. The plan of the present investigation has been to collect the cases in which pancreatic insufficiency has been proved by microscopic examination of the pancreas, to

Read at the joint meeting of the American Pediatric Society with the Society for Pediatric Research on May 5, 1938.

From the Pathological Laboratory, Babies Hospital, and the Department of Pathology, College of Physicians and Surgeons, Columbia University.

1. Holt, L. E., and Howland, J.: Diseases of Infancy and Childhood, ed. 10, edited by L. E. Holt Jr., and R. McIntosh, New York, D. Appleton-Century Company, 1933, p. 210.

2. Göttche, O.: Intestinaler Infantilismus, Jahrb. f. Kinderh. **111**:81, 1926.

study the clinical histories and associated pathologic findings and to compare these histories and findings with those in cases of celiac disease in which the pancreas appeared essentially normal on microscopic examination.

The entire series of 49 cases of pancreatic fibrosis here presented are listed in table 1. They have been obtained from four sources: 1. Twenty cases were collected from the pathologic files of the Babies Hospital. 2. One case was contributed by Dr. Bruce Chown, of the Children's Hospital of Winnipeg, Manitoba, Canada, and another by Dr. Paul Klemperer, of Mount Sinai Hospital, New York. 3. Twenty cases were collected from the literature on celiac disease and pancreatic insufficiency.[3] 4. Seven cases were collected from the literature on vitamin A deficiency.[4] The 22 new cases are designated by Roman numerals also.

3. (*a*) Landsteiner, K.: Darmverschluss durch eingedicktes Meconium; Pankreatitis, Zentralbl. f. allg. Path. u. path. Anat. **16**:903, 1905. (*b*) Kornblith, B. A., and Otani, S.: Meconium Ileus with Congenital Stenosis of the Main Pancreatic Duct, Am. J. Path. **5**:249, 1929. (*c*) Passini, F.: Pankreaserkrankung als Ursache des Nichtgedeihens von Kindern, Deutsche med. Wchnschr. **45**:851, 1919. (*d*) Gross, F.: Pankreasatrophien im Säuglings- und Kindesalter, Jahrb. f. Kinderh. **112**:251, 1926. (*e*) Benoit, W.: Hyperinsulinismus bei eingeborener Atresie des Pankreasganges, Endokrinologie **16**:313, 1935. (*f*) Tiling, W.: Angeborene Pankreasgangsatresie und Inselhypertrophie: Ein Beitrag zur Diagnostik der Pankreaserkrankungen, Arch. f. Kinderh. **106**:9, 1935. (*g*) Burghard, E.: Pankreaserkrankungen im Säuglingsalter, Klin. Wchnschr. **4**:2305, 1925. (*h*) Harper, M. H.: Two Cases of Congenital Pancreatic Steatorrhoea with Infantilism, M. J. Australia **2**:663, 1930. (*i*) Hess, J. H., and Saphir, O.: Celiac Disease (Chronic Intestinal Indigestion): A Report of Three Cases with Autopsy Findings, J. Pediat. **6**:1, 1935. (*j*) Fanconi, G.; Uehlinger, E., and Knauer, C.: Das Coeliakie Syndrom bei angeborener zystischer Pankreasfibromatose und Bronchiektasien, Wien. med. Wchnschr. **86**:753, 1936. (*k*) Siwe, S. A.: Ueber die exocrine Funktion des Pankreas und die Folgen ihres Wegfalles: Ein Fall von fast totaler Agenesie des exocrinen Teiles des Pankreas, Deutsches Arch. f. klin. Med. **173**:339, 1932. (*l*) Parmelee, A. H.: The Pathology of Steatorrhea, Am. J. Dis. Child. **50**:1418 (Oct.) 1935. (*m*) Clarke, C. G., and Hadfield, G.: Congenital Pancreatic Disease with Infantilism, Quart. J. Med. **17**:358, 1924. (*n*) Garsche, R.: Zur Klinik und Pathogenese der Pankreasinsuffizienz im Kindesalter, Ztschr. f. Kinderh. **58**:434, 1936-1937. (*o*) Huet, G. J.: A Case of Intestinal Infantilism with Chronic Pulmonary Infection, Maandschr. v. kindergeneesk. **3**:343, 1934.

4. (*a*) Blackfan, K. D., and Wolbach, S. B.: Vitamin A Deficiency in Infants: A Clinical and Pathological Study, J. Pediat. **3**:679, 1933. (*b*) Wilson, J. R., and DuBois, R. O.: Report of a Fatal Case of Keratomalacia in an Infant, with Postmortem Examination, Am. J. Dis. Child. **26**:431 (Nov.) 1923. (*c*) Corneal Ulcers and Roughened Conjunctivae Associated with Fat Intolerance, Cabot Case 17242, presented by R. W. Daffinee, with discussion by H. L. Higgins and T. B. Mallory, New England J. Med. **204**:1264, 1931.

TABLE 1.—*Summary of Cases of Cystic Fibrosis of the Pancreas in Which Postmortem Examination Was Done*

Case No.	Author	Age at Onset: Difficulty in Feeding	Age at Onset: Cough	Age at Death	Sex	Predominant Clinical Symptoms	Postmortem Observations: Cause of Death	Postmortem Observations: Data on Pancreas	Postmortem Observations: Other Data
				Group I.—Infants Dying Before the Age of One Week					
1	Landsteiner, 1905....	Birth	—	5 days	F	Vomiting; failure to pass meconium	Meconium ileus; peritonitis (Staph. aureus)	Cystic fibrosis; duct of Wirsung patent	Uric acid infarcts of kidney
2	Kornblith and Otani, 1929	Birth	—	5 days	F	Vomiting; failure to pass meconium	Meconium ileus; ulcers of ileum and colon; peritonitis	Cystic fibrosis; stenosis of duct of Wirsung	Meckel's diverticulum; atelectasis of lungs; uric acid infarcts of kidney
3 (I)	Andersen, 1938.....	Birth	—	4 days	M	Vomiting; failure to pass meconium	Band across lumen of ileum with obstruction; peritonitis	Cystic fibrosis	Meckel's diverticulum, uric acid infarcts in kidneys
4 (II)	Andersen, 1938.....	Birth	—	6 days	F	Vomiting; prematurity	Multiple atresia of ileum; volvulus; peritonitis (Str. haemolyticus)	Cystic fibrosis	Aspiration of gastric contents
5 (III)	Andersen, 1938.....	Birth	—	6 days	F	Failure to pass meconium; distended abdomen	Atresia of jejunum; fetal peritonitis	Cystic fibrosis	Congenital malformations of heart; jaundice of liver; atresia of cystic duct; congenital atelectasis of lungs
				Group II.—Infants Dying Between the Ages of One Week and Six Months					
6	Blackfan and Wolbach, case 2, 1933	Birth	Birth	5 wk.	M	Infection of respiratory tract	Bronchopneumonia; bronchiectasis	Cystic fibrosis	Keratinizing metaplasia in trachea; hemosiderosis of liver and spleen
7 (IV)	Andersen, 1938.....	Neonatal	7 wk.	8 wk.	F	Feeding problem; failure to gain	Purulent bronchitis; bronchopneumonia with abscesses (Staph. aureus)	Cystic fibrosis	Otitis media (Staph. aureus)
8	Passini, 1919, case 2..	Neonatal	?	2 mo.	F	Poor development; large stools	Bronchopneumonia; empyema	Cystic fibrosis; loss of islands	
9 (V)	Andersen, 1938.....	?	6 wk.	2½ mo.	F	Failure to gain; cough	Bronchiectasis; purulent bronchitis; lobular pneumonia (Staph. aureus)	Cystic fibrosis; atresia of Wirsung's duct ?	Atresia of cystic duct; atrophy of gallbladder; cysts of cystic duct and gallbladder; congenital strictures of ureter; congenital malformation of aorta
10 (VI)	Andersen, 1938.....	Neonatal	5 wk.	2½ mo.	M	Failure to gain; cough	Purulent bronchitis (Staph. aureus); bronchopneumonia	Cystic fibrosis; atresia of Wirsung's duct (?)	Congenital strictures of ureter; fatty liver; hemosiderosis of liver and spleen
11	Andersen, 1938.....	?	3 wk.	2¾ mo.	F	Poor development; cough	Purulent bronchitis (Staph. aureus);	Cystic fibrosis; atresia of Wirsung's	Squamous metaplasia of trachea; atresia of cystic

(VI)							bronchopneumonia	duct (?)	
11 (VII)	Andersen, 1938.....	?	3 wk.	2¾ mo.	F	Poor development; cough	Purulent bronchitis (Staph. aureus); bronchopneumonia	Cystic fibrosis; atresia of Wirsung's duct (?)	Squamous metaplasia of trachea; atresia of cystic duct (?); atrophy of gallbladder; hemosiderosis of liver and spleen
12 (VIII)	Andersen, 1938.....	?	5 wk.	2¾ mo.	F	Feeding problem; cough	Bronchiectasis, lower lobe of right lung; bronchopneumonia	Cystic fibrosis	Hemosiderosis of liver and spleen
13 (IX)	Andersen, 1938.....	?	2½ mo.	3¼ mo.	M	Pneumonia	Purulent bronchitis; abscesses of lungs; bronchopneumonia; suppurative pleurisy (Staph. aureus and Str. haemolyticus)	Cystic fibrosis	Hemosiderosis of liver
14 (X)	Andersen, 1938.....	Neonatal	6 wk.	3½ mo.	M	Prematurity; underdevelopment; cough	Purulent bronchitis; bronchopneumonia; abscesses of lungs (Staph. aureus)	Cystic fibrosis	Otitis media, right; hemosiderosis of liver and spleen
15	Gross, 1926, case 10...	?	?	3¾ mo.	?	Cachexia; bronchitis	?	Cystic fibrosis	?
16 (XI)	Andersen, 1938.....	?	3½ mo.	4 mo.	M	Malnutrition; bronchopneumonia	Acute bronchitis; bronchiectasis; lobular pneumonia (Staph. aureus and albus, B. influenzae)	Cystic fibrosis	Atresia of cystic duct (?); atrophy of gallbladder; fatty liver; otitis media; hemosiderosis of liver
17 (XII)	Andersen, 1938.....	?	2 wk.	4 mo.	F	Underdevelopment; cough	Purulent laryngitis, tracheitis and bronchitis (Staph. albus); lobular pneumonia	Cystic fibrosis; subacute pancreatitis	Prolapse of rectum; hemosiderosis of spleen
18	Blackfan and Wolbach, 1933, case 13	?	?	4 mo.	F	Failure to gain; cough; asthmatic breathing	Bronchopneumonia; chronic bronchitis and peribronchitis; bronchiectatic abscesses	Cystic fibrosis	Keratinizing metaplasia of bronchi and uterus; hemosiderosis of spleen and liver
19	Blackfan and Wolbach, 1933, case 3	1 month	1 mo.	4½ mo.	M	Failure to gain; cough; vomiting and diarrhea, following infection at age of 1 month	Bronchitis; peribronchitis; bronchopneumonia; bronchiectasis with abscesses	Cystic fibrosis	Keratinizing metaplasia of trachea; hemosiderosis of spleen
20 (XIII)	Andersen, 1938.....	Neonatal	4 mo.	4¾ mo.	F	Failure to gain; cough and fever	Acute bronchitis; bronchiectasis; bronchopneumonia	Cystic fibrosis	Atresia of cystic duct (?); atrophy of gallbladder; hemosiderosis of liver and spleen
21 (XIV)	Andersen, 1938.....	None	4 mo.	5½ mo.	M	Pneumonia	Purulent tracheitis and bronchitis; bronchiectasis; abscesses of lung (Staph. aureus); acute fibrinous pleurisy	Cystic fibrosis	Otitis media; thrombophlebitis of left lateral sinus; acute leptomeningitis; fatty liver

TABLE 1.—*Summary of Cases of Cystic Fibrosis of the Pancreas in Which Postmortem Examination Was Done*—Continued

Case No.	Author	Age at Onset: Difficulty in Feeding	Age at Onset: Cough	Age at Death	Sex	Predominant Clinical Symptoms	Postmortem Observations: Cause of Death	Postmortem Observations: Data on Pancreas	Postmortem Observations: Other Data
22	Wilson and DuBois, 1933	?	Before 3 mo.	5¾ mo.	F	Xerophthalmia; failure to gain; frequent colds	Bronchiectasis with abscesses; fibrinous pleurisy	Cystic fibrosis; keratinizing metaplasia of occasional ducts	Keratomalacia with corneal ulcers; keratinizing metaplasia in trachea, bronchi, salivary glands, pancreas, pelvis of kidney, uterus; inclusion bodies in salivary glands; hemosiderosis of liver and spleen
23 (XV)	Andersen, 1938.....	Birth	3 mo.	6 mo.	M	Failure to gain; intolerance to fat; xerophthalmia; cough	Bronchiectasis with abscesses; lobular pneumonia (Staph. aureus)	Cystic fibrosis	Lipoid pneumonia; interstitial nephritis; hemosiderosis of liver and spleen
24 (XVI)	Andersen, 1938.....	None	4 mo.	6 mo.	F	Cough; pertussis (?)	Suppurative tracheitis and bronchitis (Staph. albus haemolyticus)	Cystic fibrosis; subacute interstitial pancreatitis	Atresia of cystic duct; atrophy of gallbladder; fatty liver; hemosiderosis of spleen
				Group III.—Children Dying After the Age of Six Months					
25	Cabot case 17242, 1931	? Neonatal	6¾ mo.	7 mo.	M	"Spots in the eyes" at 4½ mo.; failure to gain	Bronchopneumonia with abscesses (Str. haemolyticus)	Cystic fibrosis; chronic pancreatitis	Keratomalacia; nephrolithiasis; atresia of cystic duct; atrophy of gallbladder
26	Blackfan and Wolbach, 1933, case 10	Birth	Birth	7 mo.	F	Failure to gain; cough since birth; attacks of fever and pyuria	Bronchiectasis with abscesses; pleurisy	Cystic fibrosis; keratinizing metaplasia of occasional ducts	Keratinizing metaplasia of mucosa of nares, trachea, bronchi, renal pelvis, ureters, periurethral glands, uterus and ducts of pancreas and submaxillary glands; hemosiderosis of liver and spleen
27	Benoit, 1935.....	Birth	?	7 mo.	F	Failure to gain since birth; foul fatty stools	Purulent bronchitis	Cystic fibrosis; atresia of ducts of Wirsung and Santorini; proliferation of duct epithelium	Hemosiderosis of spleen
28 (XXII)	Andersen, 1938..... (from Klemperer)	Birth	4 mo.	8 mo.	F	Failure to gain; intolerance to fat; cough	Purulent bronchitis; bronchiectasis with abscesses	Cystic fibrosis; cystic fibrosis of accessory pancreas in jejunum	Hyperplasia of bronchial epithelium
29	Passini, 1919, case 1..	Neonatal	?	9 mo.	?	Poor development; large stools	Bronchopneumonia	Cystic fibrosis; loss of islands	

29	Passini, 1949, case 1..	Neonatal	?	9 mo.	?	Poor development; large stools	Bronchopneumonia	Cystic fibrosis; loss of islands	
30	Blackfan and Wolbach, 1933, case 7	Birth	8 mo.	9 mo.	M	Feeding problem; projectile vomiting; cough	Bronchitis; bronchiectasis with abscesses; bronchopneumonia; fibrinous pleurisy	Cystic fibrosis	Keratinizing metaplasia of trachea, bronchi, ducts of glands of larynx, pharynx and tongue, and renal pelvis; fatty liver; hemosiderosis of spleen
31	Tiling, 1935.....	Before 5 mo.	5 mo.	9 mo.	F	Poor development; large foul stools	Purulent bronchitis; bronchopneumonia	Cystic fibrosis; atresia of ducts of Wirsung and Santorini	Hemosiderosis of spleen
32 (XVII)	Andersen, 1938.....	Neonatal	6 mo.	9 mo.	M	Failure to gain; cough	Purulent bronchitis; bronchopneumonia (Staph. aureus haemolyticus)	Cystic fibrosis; dilated pancreatic duct	Fatty liver; fatty myocardium
33	Burghard, 1925.....	Birth	About 7-8 mo.	10 mo.	F	Failure to gain; 4 to 6 foul fatty stools daily	Purulent bronchitis; lobular pneumonia	Cystic fibrosis	Fatty liver
34	Hess and Saphir, 1935, case 1	Birth	9 mo.	10 mo.	F	Poor development; frequent large foul stools from birth; large abdomen	Bronchopneumonia with abscesses	Cystic fibrosis; fat in island cells	Fatty liver; infiltration of intestinal mucosa with fibrosis of submucosa
35	Fanconi, Uelinger and Knauer, 1936, case 2	4 weeks	6½ mo.	10 mo.	?	Failure to grow; cough	Purulent bronchitis; bronchiectasis; chronic and acute bronchopneumonia	Cystic fibrosis	Fatty liver; fat in myocardium
36	Harper, 1930, case 2..	?	12 mo.	12-13 mo.	F	Failure to gain; fatty stools; diarrhea	Purulent bronchitis; bronchopneumonia	Cystic fibrosis; inclusion of embryonal tissue	Fatty liver
37 (XVIII)	Andersen, 1938.....	Birth	3 mo.	14 mo.	F	Failure to gain; large foul stools from birth	Purulent tracheitis and bronchitis; lobular pneumonia (staphylococcus and streptococcus)	Cystic fibrosis	Ethmoiditis and maxillary sinusitis; congenital anomaly of transverse mesocolon; hemosiderosis of liver and spl en
38 (XIX)	Andersen, 1938.....	3 months	14 mo.	17 mo.	F	Large foul stools; cough	Purulent bronchitis; bronchopneumonia (Staph. aureus)	Cystic fibrosis	Biliary cirrhosis; umbilical hernia; hypertrophy of colon
39	Hess and Saphir, 1935, case 2	Birth	18 mo.?	18 mo.	M	Frequent stools from birth; large foul stools after 6 mo.; vomiting; large abdomen	Bronchopneumonia with abscesses	Cystic fibrosis	Infiltration of intestinal mucosa with fibrosis of submucosa; fatty liver
40	Gross, 1926, case 18...	?	?	19 mo.	?	Heubner-Herter disease	Pneumonia	Atrophy of pancreas with replacement by fat; increase in number of islands	

TABLE 1.—*Summary of Cases of Cystic Fibrosis of the Pancreas in Which Postmortem Examination Was Done*—Continued

Case No.	Author	Age at Onset: Difficulty in Feeding	Age at Onset: Cough	Age at Death	Sex	Predominant Clinical Symptoms	Postmortem Observations: Cause of Death	Postmortem Observations: Data on Pancreas	Postmortem Observations: Other Data
41	Siwe, 1932.....	6 months	19 mo.	2 yr.	F	Prematurity; poor development; foul stools; large abdomen; cough	Varicella; pharyngitis; bronchitis	Replacement of acinar tissue by fat; atresia of Wirsung's duct with normal duct of Santorini	Rickets; mild cirrhosis of liver; fatty liver
42 (XXI)	Andersen, 1938..... (from Chown)	About 18 mo.	2¼ yr.	2½ yr.	M	Foul stools	Bronchopneumonia (staphylococcus)	Cystic fibrosis	Fatty liver
43	Fanconi, Uelinger and Knauer, 1936, case 1	Before 4 mo.	4 wk.	3 yr.	F	Failure to gain; large foul stools; cough	Bronchiectasis; purulent bronchitis	Cystic fibrosis	Osteoporosis; fatty liver; fat in myocardium; cystitis, pyelitis, interstitial nephritis
44 (XX)	Andersen, 1938.....	4 months	3 yr.	3 yr. 1 mo.	F	Poor development; intermittent diarrhea; fatty stools; hunger	Abscesses of lung; bronchopneumonia	Cystic fibrosis; atresia of Wirsung's duct (?)	Torticollis; infiltration of intestinal mucosa; fatty liver; otitis media
45	Parmelee, 1935, case 2	Neonatal	3 yr. 10 mo.	4 yr.	F	Failure to gain; large stools; intolerance to fat	Mucopurulent bronchitis and bronchiolitis; lobular pneumonia with abscesses	Cystic fibrosis; narrow pancreatic duct	Atresia of cystic duct (?); atrophy of gallbladder; fatty liver; narrow common and hepatic bile ducts
46	Clarke and Hadfield, 1924	Birth	?	4½ yr.	F	Poor development; fatty stools from birth; large abdomen; hunger	Purulent bronchitis; bronchopneumonia; abscesses of lung	Replacement of acinar tissue by fat	Large colon with infiltration and fibrosis of submucosa; ulcer of ileum; fatty liver; edema of extremities
47	Garsche, 1936-1937, case 3	6 months	4⅓ yr.?	4⅓ yr.	F	Failure to gain; large foul stools; protuberant abdomen; alternate hunger and anorexia	"Grip" pneumonia	Fibrosis; replacement of acinar tissue by fat; concrements	Fatty liver; mild biliary cirrhosis of liver
48	Huet, 1934.....	Nursing period	6 yr.	10 yr.	M	Poor development; fatty stools; chronic infection of lung	Purulent bronchitis with dilatation of bronchi; fibrosis of lung	Cystic fibrosis; hyperplasia of islands	Cirrhosis of liver (Laënnec's); fatty liver
49	Parmelee, 1935, case 1	Early infancy	11 yr.	14½ yr.	F	Feeding problem; rancid fatty stools; intolerance to fat; hunger; protuberant abdomen; maxillary sinusitis; chronic bronchitis; anemia	Purulent bronchitis; acute bronchopneumonia	Cystic fibrosis with normal ducts	Maxillary sinusitis; fibrinous pericarditis; ascites

CLINICAL PICTURE

A perusal of the clinical histories reveals the unexpected fact that the cases form three groups, which differ in their clinical features and in the age at which death occurred (table 1). The first group includes newborn infants; the second, infants from 1 week to 6 months of age, and the third, all those over 6 months of age. In all cases the pancreas at death showed such extensive lesions of the acinar tissue that it is inconceivable that the external secretion of the pancreas could have been produced in normal volume.

Group I.—This group consists of cases of 5 infants all of whom were born at term and died before the age of 1 week with symptoms of intestinal obstruction. In the 2 cases quoted from the literature [5] the

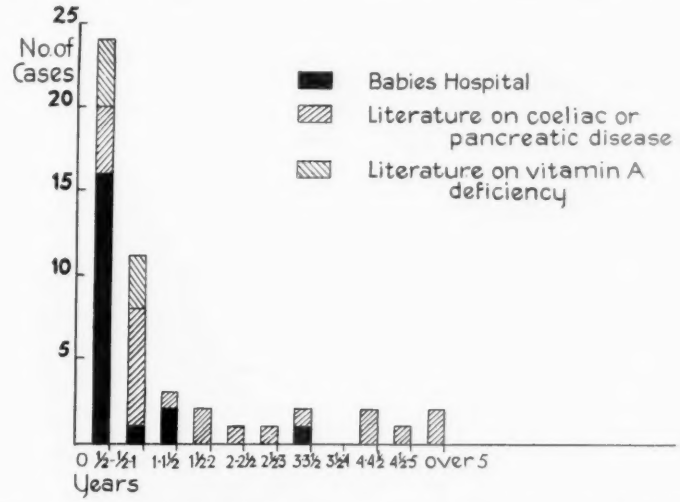

Fig. 1.—Chart showing the age at death in 49 cases of cystic fibrosis of the pancreas. The shading of the columns indicates the sources from which the cases were collected.

obstruction appeared to be due to inspissated meconium without any break in the continuity of the intestinal lumen. In 1 there was staphylococcic peritonitis and in the other meconium peritonitis resulting from perforation of the ileum. There was stenosis of the duct of Wirsung in 1 case [3b] but not in the other.[3a] Reports on the remaining 3 cases of this group were found in the pathologic files of the Babies Hospital. In case 3 (I) the obstruction was due to a band of fibrous tissue across the lumen of the terminal portion of the ileum near the ileocecal valve. In the other 2 cases (cases 4 [II] and 5 [III]) the obstruction was due to atresia of the jejunum and of the ileum, respectively. Fetal

5. Landsteiner,[3a] Kornblith and Otani.[3b]

peritonitis was present in the 3 latter cases. In all 5 of the cases the pancreas showed extensive fibrosis with the formation of cysts. The following associated congenital anomalies were found in 3 of the 5 cases: Meckel's diverticulum (2 cases), atresia of the cystic duct (1 case) and congenital malformation of the heart (patent interventricular septum), in case 5 (III). An extensive search through the literature has revealed no additional instance of atresia of the small intestine in which the pancreas showed cystic fibrosis, and the frequency of this association is unknown. The files of the Babies Hospital contain 1 case of intestinal atresia in which the pancreas was normal on microscopic examination. However, the literature contains several cases of atresia of the duodenum with hypoplasia of the pancreas.[6] Kornblith and Otani [3b] stated the opinion that in their case and in that of Landsteiner [3a] the absence of pancreatic juice caused inspissation of meconium with subsequent intestinal obstruction. The atresia of the intestine in 2 cases cannot be explained in this way. The possibility that the atresias of the intestine, of the cystic duct and of the large and small pancreatic ducts are due to a common cause will be discussed later in the present paper.

Group II.—The cases of 19 infants who died between the ages of 1 week and 6 months form this group. Two of these cases were found in the literature on celiac disease and 4 in that on vitamin A deficiency, and the remaining 13 are reported for the first time in this paper. In all of them the pancreas showed cystic fibrosis, and comparison of the microscopic slides and descriptions revealed a close similarity in the various cases. The characteristic features of the clinical picture may be summarized as follows: (1) failure to gain with an adequate diet, beginning in the neonatal period; (2) a large abdomen at birth; (3) hunger; (4) absence of vomiting or diarrhea; (5) large stools, sometimes recognized as fatty; (6) intolerance to fat in the diet, and (7) chronic infection of the respiratory tract.

Clinically there are two subgroups: (*a*) The larger number of cases are those of patients who were first seen because they presented a nutritional problem or because, having been admitted on account of infection of the respiratory tract, they were found on investigation to be retarded in growth and development. (*b*) Six cases, all of which are described here for the first time, are those of patients who were brought to the hospital because of infections of the respiratory tract, and gave no history of previous nutritional difficulty.

In subgroup *a*, comprising 13 cases in which the feeding problem was recognized, the presenting symptom was usually failure to gain,

6. Niosi, G. S.: Atresie multiple congenite del duodeno e del dijiuno accociate ad assenza della cistifellea e ad ipoplasia d'alto grado del pancreas, Pathologica **28**:414, 1936.

first noticed during the neonatal period; in some cases there were large foul stools from birth. Dr. Katharine Merritt made a study of the charts of the patients in the Babies Hospital, and I have her assurance that the feeding was adequate in quantity and quality, as nearly as could be ascertained. Repeatedly one met the comment that the infant seemed hungry and consumed with relish anything that was given. Vomiting was rare, except during the course of an infection. There was often a mild increase in the number and size of the stools, which occurred from two to six times daily, but they were not characteristically diarrheal and were only occasionally recognized as fatty stools during this age period. No analysis of fat in the stools was recorded before the age of 6 months. Occasionally it was noticed that the baby was intolerant of fat (case 23 [XV]) or of cereals (case 44 [XX]). Physical examination revealed underdevelopment and poor nutrition (fig. 2 *A, B*). Often, but not always, the abdomen was enlarged, and sometimes an umbilical hernia was present. Xerophthalmia was found in 2 infants.

In each of the 19 cases comprising group II there was ultimately an infection of the respiratory tract. This sometimes began with coryza, but more often the symptom first noticed was a spasmodic, nonproductive cough resembling that of pertussis and often so interpreted. The age at which this cough appeared ranged from 2 weeks upward; it is recorded for the individual cases in table 1. For weeks or months it remained as a chronic cough, gradually increasing in severity, with development of purulent bronchitis, bronchiectasis with abscesses, lobular pneumonia or any combination of these conditions. In 2 cases roentgenograms made soon after the onset of cough revealed no abnormality in the lungs (cases 14 [X] and 23 [XV]), but there were roentgen evidences of bronchopneumonia in all of the 12 cases in which the patients were examined late in the course of the disease. In several cases the transition from a condition marked only by chronic cough to purulent bronchitis was sudden.

The laboratory findings in the cases of group II did not contribute much to an understanding of the disease. There was no clinical or pathologic evidence of syphilis in any case. When serologic tests were done the reactions were negative (7 cases). The blood of the mother of 1 infant (case 10 [VI]) gave a positive Wassermann reaction; the infant's serum was not tested, but autopsy showed no morphologic evidence of syphilis. The hemoglobin content ranged from 8.5 to 23 Gm. per hundred cubic centimeters of blood, usually lying between 10 and 14 Gm. The red blood count ranged from 2,300,000 to 5,600,000 and was usually between 3,000,000 and 4,500,000. The observations were made after the infection of the respiratory tract

had appeared, and the anemia cannot with assurance be attributed to the pancreatic insufficiency. The urine was normal or showed a trace of albumin, except in case 23 (XV), in which there was pyuria. The blood sugar was determined in 1 case only; it was 75 and 87 mg. per hundred cubic centimeters on two occasions (case 23 [XV]). In the same case the stools were cultured for the typhoid and dysentery group of

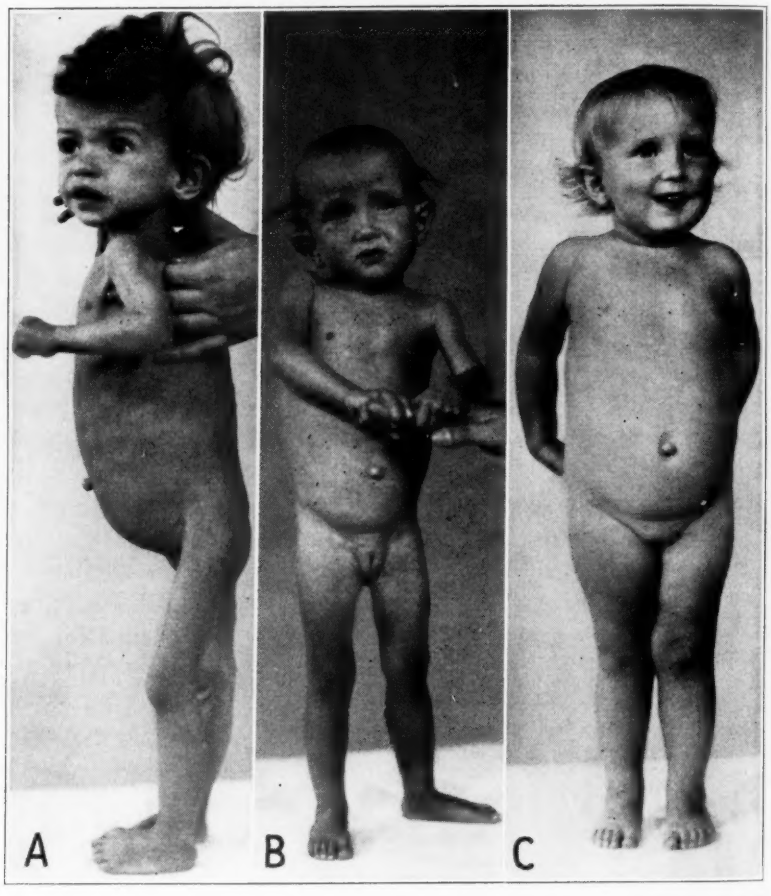

Fig. 2.—*A*, C. H. (case 37 [XVIII]) at the age of 1 year; *B*, M. D. (case 44 [XX]) at the time of admission to the hospital at the age of 22 months, and *C*, M. D. at the age of 3 years.

organisms, with negative results, and no agglutinins against these organisms were found in the blood. The stools were not examined for fat. Roentgen study demonstrated bronchopneumonia, osteoporosis of the shafts and epiphyses and absence of rickets.

I have found no obvious solution for the apparent clinical discrepancy between these two subdivisions of group II, one of which showed predominantly a nutritional disturbance and the other an infection of the respiratory tract; the two subgroups had in common the characteristic postmortem lesions of the pancreas and of the respiratory tract. One may attempt to explain the occurrence in the cases of subgroup II *b* of cystic fibrosis of the pancreas in the absence of serious and easily recognizable disturbances of digestion and nutrition during life by any one of four theories: 1. The lesion in the pancreas may be incidental and unrelated to the clinical picture caused by the lesions in the bronchi and lungs, as suggested by Blackfan and Wolbach.[4a] 2. The changes found in the pancreas may be responsible for the digestive and nutritional symptoms when these have occurred, but in some cases their appearance may have been delayed by some undetermined factor, such as breast feeding. 3. Symptoms which one would expect to result from the pancreatic lesion may have been present but unnoticed because the infant did not appear ill. 4. Symptoms specifically referable to deficiency of the external secretion of the pancreas may have been obscured by the early onset of the infection of the respiratory tract and attributed to the latter cause. The theory first suggested appears improbable, in view of the fact that every patient surviving the age of 6 months showed symptoms suggestive of celiac disease. The second theory is possibly true, but this also appears unlikely. Although 5 of the 6 infants in the cases of group II*b*, who did not present a feeding problem, were breast fed and might be thought to have been thus protected, there were 3 infants in the cases of group II*a* who were changed from breast feeding because of failure to thrive on it, which indicates clearly that nursing does not constitute a safe guaranty per se against the development of the nutritional disturbances. Moreover, there was no constant difference betwen the growth curves of the breast-fed and those of the artificially fed infants. The third possibility, that the failure to gain went unnoticed because the infants were active and ate well, is a likely one and is borne out by the fact that all children but 1 in the entire series were much below normal in weight and development when first seen. Finally, in favor of the fourth interpretation stands the fact that all 6 of the infants in group II*b* were admitted with acute pneumonia; attention was focused on this, and the subnormal weight was reasonably attributed to the infection.

Group III.—The group is composed of 25 cases of patients who ranged in age at death from 6 months to 14½ years. A nutritional disturbance was recognized clinically in all cases, and a diagnosis of celiac disease was made in most instances. The diagnosis of pancreatic insufficiency was made during life in 4 cases (case 27, 31, 41, 37

[XVIII]). The pathologic changes in the pancreas were similar to those in the previous cases with 4 exceptions: In the cases of Gross (his case 18),[3d] Clarke and Hadfield,[3m] Siwe [3k] and Garsche,[3n] the acinar tissue was entirely replaced by adipose tissue.

In group III the clinical course in the first months of life was similar to that in the cases of group II. The initial symptom was failure to gain, usually first noticed in the neonatal period and almost always present by the fifth month. Case 42 (XXI) is the single exception to this, for no abnormalities either in development or in digestive functions were noted until occurrence of the acute illness, at about the age of 16 months. In all the other cases there were large foul stools, sometimes recognized as fatty, beginning at birth or thereafter but always present by the sixth month. One gathers from reading the protocols that the abnormality in the stools became more obvious at about the sixth month and that it was then recalled that they had been somewhat abnormal previously. The change in type of stool at 6 months was sometimes specifically recorded.[7] The underdevelopment was also more striking than in the previously described cases of group II. Physical examination revealed the findings described for celiac disease: underdevelopment, a protuberant abdomen, often an umbilical hernia, weakness of the muscles and atrophy of the gluteal region. Osteoporosis was frequently described, but rickets was rarely found.[3k] Xerophthalmia was found once.[4e] The terminal event, in these as in the previous cases, was infection of the respiratory tract: bronchitis, bronchiectasis or bronchopneumonia, often with otitis media and sometimes with infection of the accessory nasal sinuses.

Laboratory findings were recorded in only a few of the reports. Anemia was sometimes mentioned, but in 3 of the 4 cases of the Babies Hospital it was not present prior to the infection of the respiratory tract. The examination of the blood and urine did not otherwise give significant results. The stools were usually described as pale or putty colored, extremely foul, rancid, soft and pasty. In 2 cases (cases 37 [XVIII] and 44 [XX]) cultures were negative for typhoid and dysentery bacilli on repeated occasions. In 1 case (35) 52 per cent of the protein and 50 per cent of the fat ingested were discharged in the stool. In most cases microscopic examination showed no droplets of neutral fat, but these were present in the cases of Burghard,[3g] Siwe [3k] and Clarke and Hadfield.[3m] The stool was analyzed for fat in 4 cases: In Harper's case [3h] the stool contained 60 per cent of fat in the dried weight, of which 76.6 per cent was fatty acid; in case 37 (XVIII) the stool contained 39.8 per cent of fat in the dried weight, of which 64 per cent was fatty acid; in case 44 (XX) the stool contained 53.5 per cent

7. Harper.[3h] Clarke and Hadfield.[3m] Garsche.[3n]

of fat in the dried weight, of which 69 per cent was fatty acid; Siwe [3k] found 82 per cent and 96 per cent of the total fat as neutral fat on two occasions. The proportion of fatty acid to total fat was therefore within normal range in 3 cases but extremely low in 1. It is of interest that in the first 3 cases the pancreas showed cystic fibrosis, while in Siwe's case [3k] there was complete replacement of the acini with adipose tissue.

The blood sugar value was low in several cases (3 from the literature [8] and cases 37 [XVIII] and 44 [XX] from the Babies Hospital), and spontaneous attacks of hypoglycemia have been described.[9] Dextrose tolerance tests were done in 4 cases. In 2 (Siwe,[3k] case 44 [XX]) there was a rise from a low fasting level to over 200 mg. per hundred cubic centimeters in an hour, with an abrupt drop at two hours. These curves are similar to those described by Harris [10] as characteristic of hyperinsulinism. In a third case (Huet [3o]) the fasting level was 140 mg., rising to 204 mg. in an hour and dropping to 138 mg. in two and one-half hours. In the fourth case (case 37 [XVIII]) the curve was flat, as with celiac disease. In case 37 (XVIII) the serum cholesterol value was low (total 107, free 36.6, combined 70.4 mg. per 100 cubic centimeters, ratio of combined to free, 1.92). The amount of serum lipase (tributyrinase) was normal in this case, and that of serum amylase was about four times normal. The duodenal contents were examined for the presence of pancreatic ferments (diastase, trypsin, and lipase) in 3 cases, and none was found.[8]

PATHOLOGIC ANATOMY

Gross Examination.—The postmortem findings in the 5 cases of group I have been described. The following comments apply to the remaining 44 cases unless otherwise stated.

External Examination: The underdevelopment seen clinically was also obvious at autopsy, together with emaciation and muscular atrophy. The abdomen was usually prominent and there was often umbilical hernia. Rectal prolapse was observed twice. Congenital torticollis was noted once.

Body Cavities: The peritoneal cavity bore a smooth serosa. There was often moderate distention of the intestines, with some enlargement and hypertrophy of the colon. The liver was frequently enlarged to a moderate degree, extending below the costal margin. The pericardial cavity was normal except in 1 case, in which there was fibrinous peri-

8. Benoit.[3e] Tiling.[3f] Siwe.[3k]

9. Benoit.[3e] Tiling.[3f]

10. Harris, S.: Gastrointestinal Manifestations of Hyperinsulinism, Am. J. Digest. Dis. & Nutrition **2**:557, 1935.

carditis.[31] Fibrinous pleurisy was almost invariably observed. Suppurative pleurisy was described in 3 cases and fibrous thickening of the pleura in 1 case.

Heart: Fatty infiltration of the myocardium was noted in 3 cases. With the exception of a patent interventricular septum in 1 of the cases of group I and several instances of slight patency of the foramen ovale

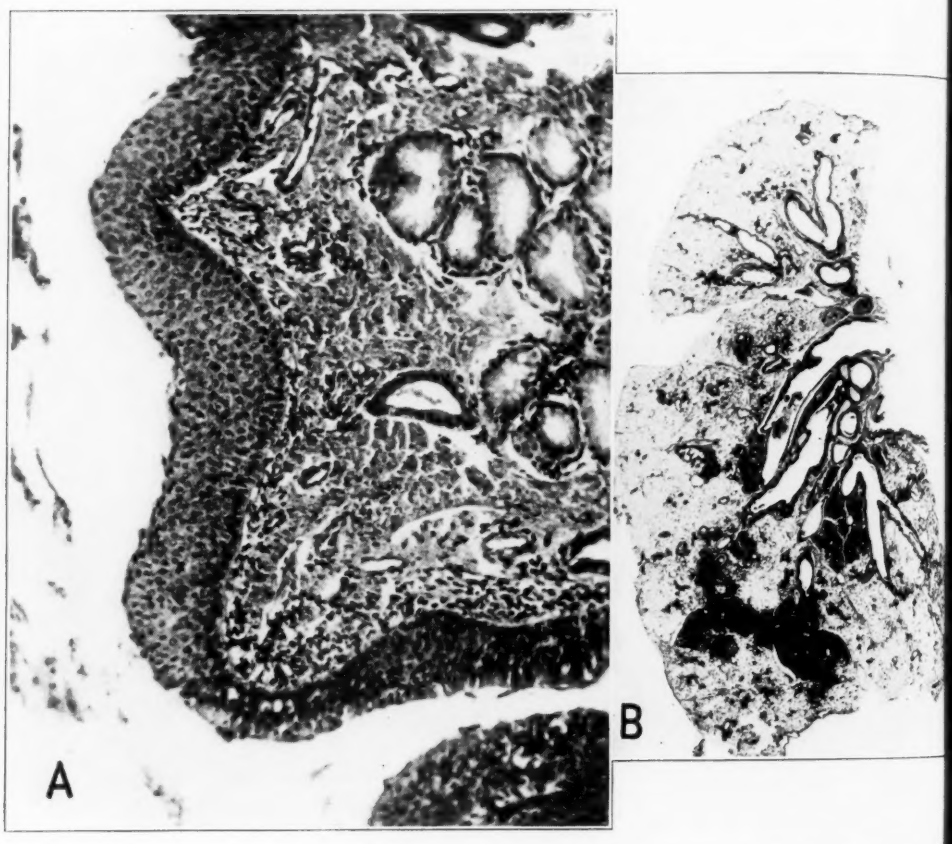

Fig. 3.—*A* (case 11 [VII]), photomicrograph showing squamous metaplasia of tracheal epithelium. *B* (case 20 [XIII]) shows tubular bronchiectasis, purulent bronchitis and bronchopneumonia.

or ductus arteriosus, there were no congenital malformations of the heart.

Aorta: A congenital abnormality of the origin and course of the right subclavian artery was seen in case 9 (V). No other abnormalities were noted.

Lungs: In every case of the series there was infection of the lungs; this was apparently primary in the bronchi. In the cases which I

have been able to study at first hand, these changes were remarkably uniform and consisted of (1) mild tubular dilatation of the small bronchi and bronchioles; (2) plugging of the lumens of most if not all of the bronchi with tenaceous, greenish gray mucopurulent material; (3) multiple small abscesses arising in the smaller bronchi and sometimes spreading to form multilocular abscesses; (4) fresh lobular pneumonia in the intervening parenchyma; (5) perforation of the abscesses through the pleura to produce fibrinous or suppurative pleurisy (fig. 3*B*). The larger bronchi and trachea also contained mucopurulent material, with some congestion of the underlying mucosa. In Huet's case,[3o] in which the pulmonary infection was especially prolonged, there was some fibrosis of the lung.

Spleen: This was normal or slightly enlarged, with small malpighian corpuscles and red pulp. In 1 case, in which there was cirrhosis of the liver,[3o] the spleen was large and somewhat fibrous.

Liver: A fatty liver, noted in 19 cases, was more frequently met with in the children over 6 months of age (21 per cent of group II, 60 per cent of group III). The liver was enlarged in these cases but not in the others. Usually it had a brownish tinge. In some of the smaller infants it was dark red. Biliary cirrhosis was present in 3 cases and Laënnec's cirrhosis in 1.

Gallbladder and Bile Ducts: In 8 cases, including 1 of group I, the gallbladder was small and contained only a small amount of translucent gray mucus. The cystic duct was atretic in 4 of these cases and was not examined in the other 4, but it is reasonable to assume that it was atretic in them also. Six or 30 per cent of the cases of the Babies Hospital presented this finding. No abnormalities of the common or hepatic ducts were noted.

Pancreas: In most instances no gross abnormalities were detected. Siwe [3k] and Clarke and Hadfield [3m] observed the fatty infiltration, which they confirmed microscopically. Sensitized by my previous experience with this disease, I have been able to make a gross diagnosis in recent cases. The pancreas was normal in size or somewhat small, and the shape and color were normal. On section it was firm, sometimes more so than normal, and occasionally there was a slight grating sound as the knife passed through calcified concretions. The lobules appeared rounded and uneven in size instead of having the normal diamond-shaped pattern. Many lobules were fused together by fibrous tissue. The pancreatic duct was examined in 12 of the 49 cases. It was described as atretic in 3 cases;[8] there was stenosis near the orifice in 2.[11] Attempts to dissect out the duct were unsuccessful in 4 of 5 of the cases of the Babies Hospital, in all of which the lumen appeared to end

11. Kornblith and Otani.[3b] Parmelee.[31]

in fibrous tissue at a distance of 5 to 15 mm. from the ampulla of Vater. In 1 of these cases the duct of Santorini was readily dissected, though narrow. Because of the difficulty of dissecting the pancreatic duct in small infants, the failure to do so is not considered as absolute proof that the duct was atretic. In 2 cases (Landsteiner,[3a] case 32 [XVII]) the duct was patent, and in case 32 it was dilated throughout. In 1 case it was described as normal.[3l]

Adrenal Glands: No abnormalities were noted.

Kidneys and Ureters: There was congenital stricture of the ureters with mild hydronephrosis in cases 9 (V) and 10 (VI). Nephrolithiasis was reported once.[4c] In 2 cases the kidneys showed mild chronic interstitial nephritis (Fanconi and others,[3j] case 23 [XV]).

Pelvic and Reproductive Organs: No abnormalities were noted.

Alimentary Tract: Moderate distention of the small intestine and dilatation and hypertrophy of the colon were occasionally recorded. There were ulcers of the ileum in 1 case.[3m] Rectal prolapse was recorded twice.

Middle Ears and Accessory Nasal Sinuses: No notes were found in the pathologic reports in the literature. Parmelee [3l] recorded chronic sinusitis in his first case and otitis media in the second case as clinical findings. Otitis media was observed in cases 14 (X), 16 (XI), 21 (XIV) and 44 (XX) and maxillary sinusitis in case 37 (XVIII) of the series of the Babies Hospital.

Additional Findings: In case 21 (XIV) there was thrombophlebitis of the left lateral sinus, with leptomeningitis.

Microscopic Examination.—Heart: No abnormalities were noted other than those described grossly.

Aorta: This was rarely mentioned and may be considered normal.

Lungs: The bronchi presented the changes of greatest interest. Bronchitis and peribronchitis were found in all cases, and the bronchial lumens were filled with purulent exudate. In addition, the epithelium of the bronchi was often composed of more cell layers than usual, and in the cases reported in the literature on vitamin A deficiency there was squamous metaplasia of the superficial layers with keratinization.[4] In 1 of the cases of the Babies Hospital (case 11 [VII]) and in the case contributed by Dr. Klemperer (case 28 [XXII]) there was likewise squamous metaplasia, but careful search did not reveal it in the other cases of the Babies Hospital. There was moderate to marked tubular dilatation of the bronchi in all of the cases of the Babies Hospital, and bronchiectasis was frequently reported in the literature (fig. 3*B*). In most of the cases of the Babies Hospital there were abscesses arising in the smaller bronchi, as shown by fragments of bronchial walls present in or near them and by their location. Staphylococci were seen in the

necrotic centers. The alveoli showed patchy, usually very recent, lobular pneumonia, with normal or emphysematous areas between the consolidated ones. In 1 case [30] there were areas of fibrosis. The pleural surface bore a fibrinous or fibrinopurulent exudate.

Trachea: There was squamous metaplasia with keratinization in 5 of the cases reported as instances of vitamin A deficiency and in case 11 (VII) (fig. 4). Purulent tracheitis was frequently reported.

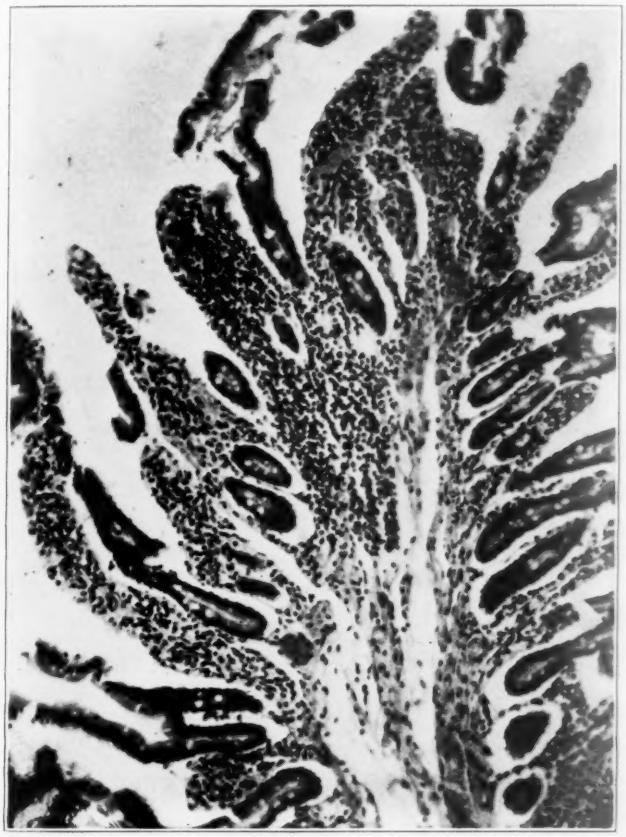

Fig. 4 (case 44 [XX]).—Photomicrograph of jejunal mucossa.

Spleen: The malpighian corpuscles were usually small; the pulp was congested and contained greater or lesser amounts of hemosiderin. Polymorphonuclear leukocytes were often present in small numbers.

Liver: Hemosiderin in the liver and in the Kupffer cells was almost invariably observed. Large amounts of fat were present in the cells in a large percentage of the cases. Biliary cirrhosis was noted 3 times, and in several of the cases of the Babies Hospital there was a slight

increase of fibrous tissue in the portal areas. Laënnec's cirrhosis was seen once.[30] In several of the cases of the Babies Hospital there was slight atrophy of the columns of cells, with congestion of the sinusoids. In 2 instances multinucleated hepatic cells were observed.

Gallbladder and Bile Passages: These were rarely examined histologically. There were small epithelial cysts containing mucus and

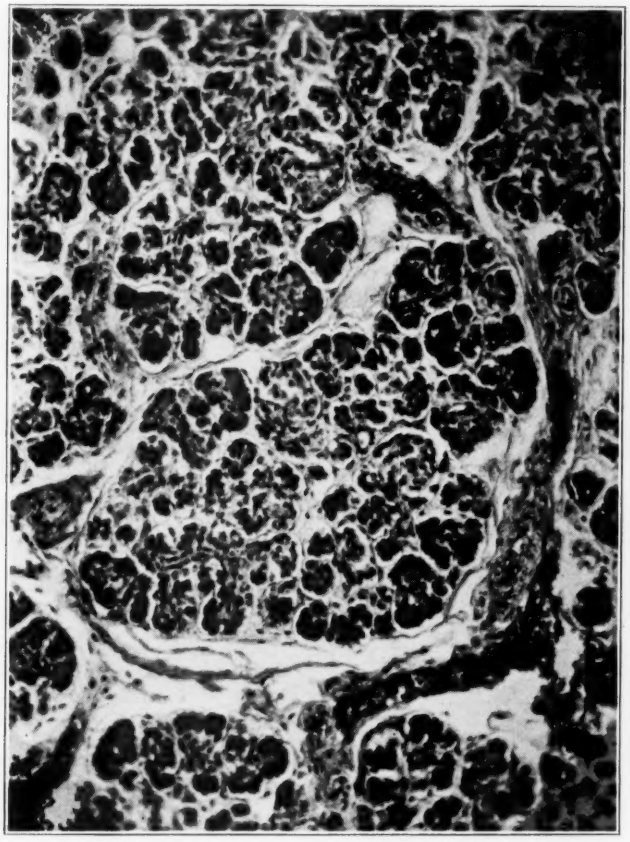

Fig. 5.—Photomicrograph of normal pancreas of a patient who died at the age of 3 days.

apparently arising from the mucous glands in the gallbladder and in the cystic duct in case 9 (V).

Adrenal Glands: No abnormalities were noted.

Pancreas: In 45 of the cases the pancreas presented a microscopic picture which is described by the term "cystic fibrosis" (figs. 5 to 11). The acini contained concretions of various sizes, and the acinar cells were flattened to form a thin epithelial wall around them. The smaller concretions were surrounded by relatively normal cells, which occa-

sionally contained eosinophilic granules. The flattening of the epithelium varied approximately with the size of the concretions. The small ducts contained similar material and were often difficult to distinguish from the acini. Metaplasia of the epithelium of occasional ducts was described.[12] The concretions themselves were more or less deeply eosinophilic. The smaller ones were homogeneous; the larger were often laminated and were sometimes composed of fragments of deeply

Fig. 6 (case 4 [III]).—Photomicrograph of pancreas of a patient who died at the age of 6 days.

eosinophilic material surrounded by a paler substance; occasionally they were calcified. Sometimes there were desquamated epithelial cells, one or two phagocytes or a rare polymorphonuclear leukocyte in the cysts which contained the paler material. The size of the cysts varied in each case, but large ones were not often noted in the youngest infants. Surrounding the acini and also the lobules there were moderate to large

12. Huet.[30] Blackfan and Wolbach.[40]

amounts of fibrous tissue, the quantity varying roughly with the age of the child. This sometimes contained a few fibroblasts or young fibrocytes and was always infiltrated with lymphocytes, plasma cells and phagocytes. These varied in number from occasional scattered cells to a number sufficient to warrant the diagnosis of subacute or chronic pancreatitis. In the latter case occasional polymorphonuclear leukocytes

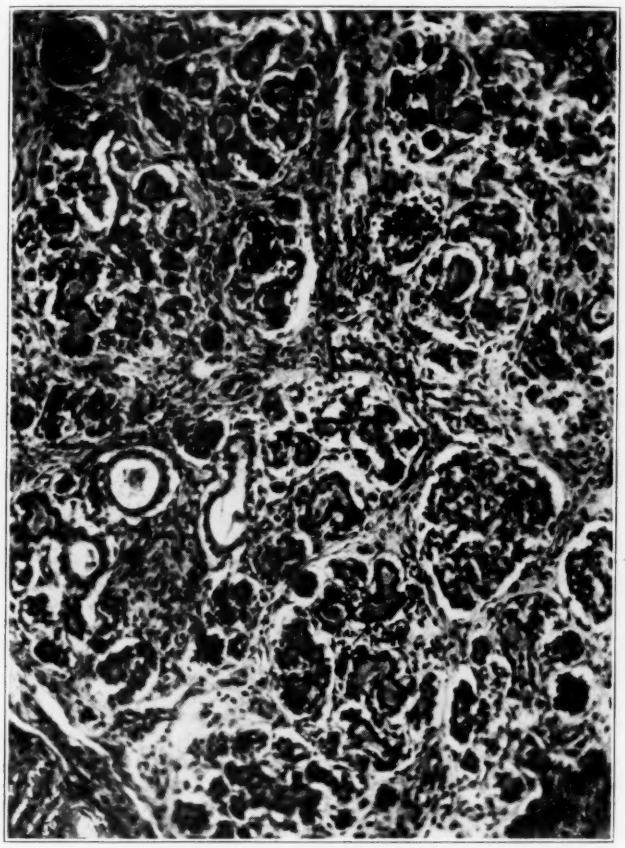

Fig. 7 (case 7 [IV]).—Photomicrograph of pancreas of a patient who died at the age of 8 weeks.

were observed. These infiltrations were diffuse and did not bear a consistent relation to the ducts. The islands of Langerhans were usually normal in number and appearance, although they were considered to be decreased in number in several cases.[13] Hess and Saphir [3i] observed fat in the island cells in 1 case. In several cases the islands retained their connection with adjacent acini or ducts but appeared normal in other respects. In Harper's case [3h] a mass of embryonal tissue was seen.

13. Passini.[3c] Gross.[3d] Tiling.[3f] Huet.[3o]

The acinar tissue was absent and was replaced by adipose tissue in four cases,[14] as shown in the illustrations in Siwe's paper.

Kidney and Ureters: Keratinizing metaplasia in the renal pelvis was described in 3 cases [15] and in the ureter in 1 case. These are not the cases already mentioned as those in which there were ureteral strictures and in which the ureters were unfortunately not examined

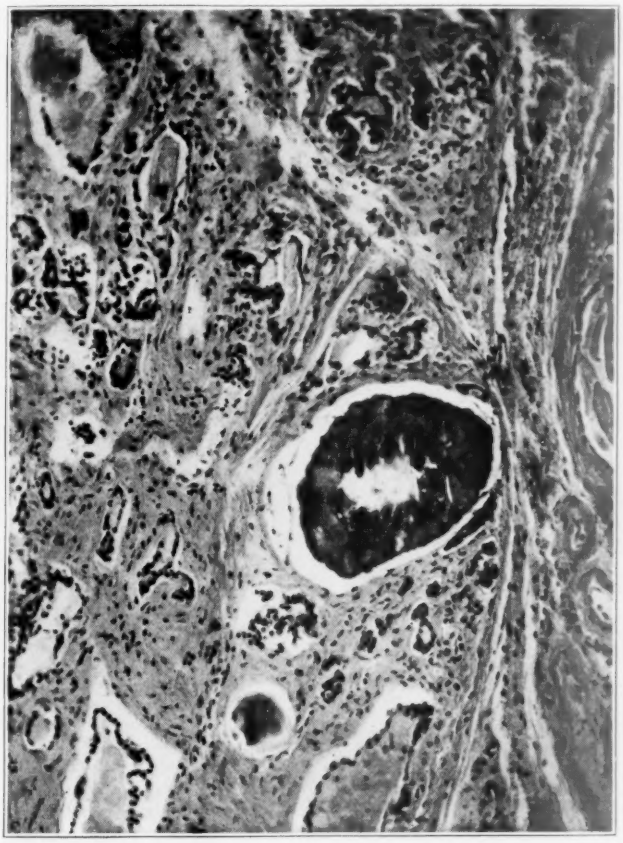

Fig. 8 (case 37 [XVIII]).—Calcified concretion in the pancreas of a patient who died at the age of 14 months.

microscopically. Mild chronic interstitial nephritis was observed in case 23 (XV).

Pelvic and Reproductive Organs: Keratinizing metaplasia of the uterine mucosa was described in 3 cases.[15] The periurethral glands showed similar changes in 1 case.

14. Gross.[3d] Siwe.[3k] Clarke and Hadfield.[3m] Garsche.[3n]
15. Blackfan and Wolbach.[4a] Wilson and Dubois.[4b]

Alimentary Tract: The esophagus and stomach were rarely mentioned, and no abnormalities were noted. A moderate infiltration of lymphocytes, plasma cells and occasional polymorphonuclear leukocytes was seen in the intestinal mucosa in 3 cases, and fibrosis of the submucosa was also present (Hess and Saphir,[3i] Clarke and Hadfield,[3m] case 44 [XX]). These children were aged 10 months, 18 months and 4½ years respectively. In most cases the intestine appeared normal.

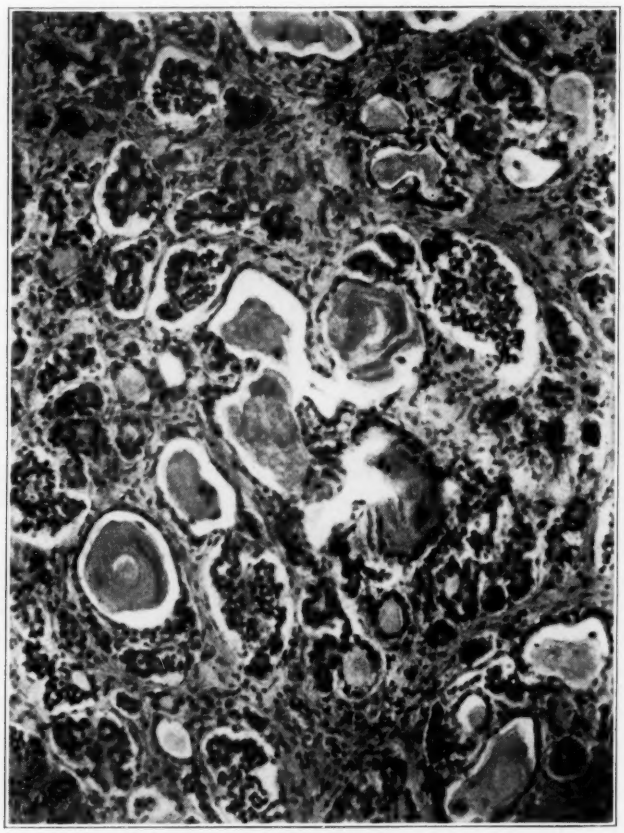

Fig. 9 (case 38 [XIX]).—Photomicrograph of pancreas of a patient who died at the age of 17 months.

Additional Findings: Keratinizing metaplasia was reported in the submaxillary gland and in the ducts of the glands of the tongue and larynx.[15] Inclusion bodies and some cellular infiltration were noted in the salivary glands.[4b]

Bacteriology.—Cultures were reported in 15 of the 49 cases. In 9 of them a pure culture of Staphylococcus aureus was obtained from the lung or pleura and in 1 from the peritoneum.[3a] Other cultures of

material from the lung showed Staphylococcus albus (2 cases), Streptococcus haemolyticus (1 case) or mixed infections in which Staph. aureus was present (3 cases).

ETIOLOGY

Frequency of Cystic Fibrosis of the Pancreas.—The performance in the laboratory of the Babies Hospital of 4 autopsies on patients with

Fig. 10 (case 44 [XX]).—Photomicrograph of pancreas of a patient who died at the age of 3 years.

cystic fibrosis of the pancreas in a period of less than a year suggests that this lesion is not so rare as the scarcity of reports in the literature would lead one to believe. Microscopic sections of the pancreas were made in 605 of the last 1,000 autopsies in the Babies Hospital, and a survey of these sections was undertaken. The sections containing cysts were classified into three groups according to the estimated amount of acinar tissue involved. There were 20 cases or 3.3 per cent in which 90 per cent or more of the acinar tissue appeared to be nonfunctioning, and

these cases form the basis of this paper. In 21 or 3.5 per cent the lesion occupied approximately 20 to 90 per cent of the tissue. Three of the patients in these cases had histories similar to those of the first group, but the remainder died of a variety of causes. In 69 cases or 11.4 per cent there were smaller numbers of cysts, and these cases also form a miscellaneous group. In my experience the syndrome described in this paper is present only when the major portion of the acinar tissue

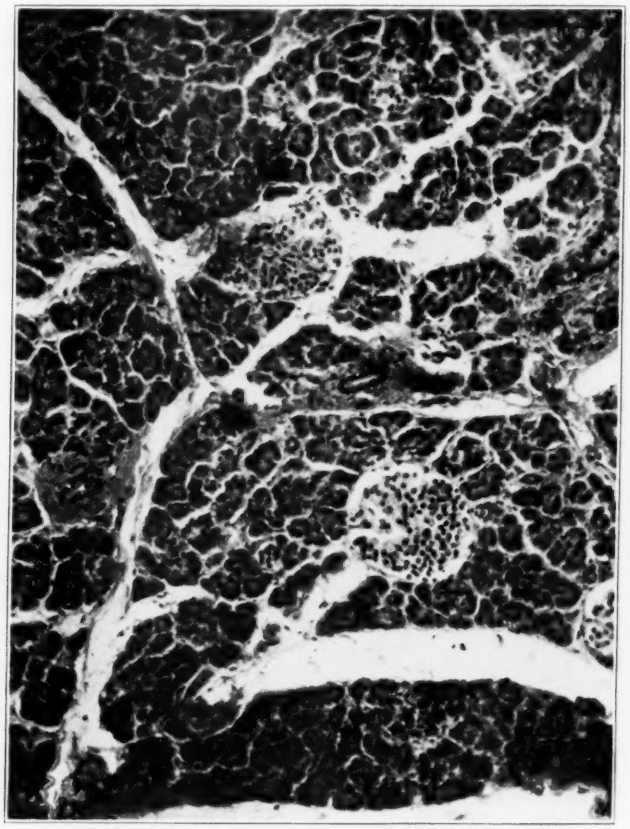

Fig. 11.—Photomicrograph of normal pancreas of a patient who died at the age of 3 years.

appears to be nonfunctioning. The incidence of 3.3 per cent seems unusually high for a disease so little known. The explanation probably lies in the fact that until recent years it has not been the custom to examine every pancreas microscopically. In cases of infants dying of bronchopneumonia in which neither the clinical history nor the gross examination had suggested a pancreatic lesion, sections of this organ were often not made. This explanation is supported by the fact that the

majority of the cases in which death occurred before the sixth month were culled from the autopsy records of the Babies Hospital, whereas most of the cases in which the patients survived longer were collected from the literature; in the latter the clinical history was suggestive of celiac disease. It is suggested that the disease occurs with approximately the frequency presented in my analysis but that the infants do not often survive to an age when the nature of the symptoms during life has instigated a postmortem study of the pancreas.

Sex.—The sex was recorded in 45 cases, in 30 (67 per cent) of which it was female and in 15 male.

Familial Occurrence.—The family history was given in 36 cases. In 3 instances 2 siblings of the family were found by postmortem examination to have cystic fibrosis of the pancreas (Passini,[3e] Blackfan,[4a] cases 23 [XV] and 28 [XXII]). In 5 other instances an older sibling was said to have died in early infancy of some congenital disease after a course similar to the patient's, but no postmortem examination was made (Tiling,[3f] Harper,[3h] Fanconi and others,[3j] (cases 7 [IV] and 12 [VIII]). In 2 of these cases the patients also had siblings who were living and well. In 15 cases there were normal siblings only, and in 10 cases the patient was the result of the first pregnancy. If only those families are considered in which there were siblings, the following figures appear: The disease is proved to have occurred more than once in 3 of 23 families and may have so occurred in 5 more. It is of interest that the mother in the 2 cases of Blackfan and Wolbach was intolerant to fat in the diet; the 2 infants were twins. Burghard's patient [3g] had a normal twin.

Race and Distribution.—The cases are reported from Germany, England, Holland, Australia and Canada and from the East, the Middle West and the West Coast of the United States. One of the patients of the Babies Hospital was a Negro, and the parents of the others came from Puerto Rico, Italy, Germany, Ireland and various parts of the United States. Patients were found to come from various economic strata.

Pathogenesis of the Pancreatic Lesions.—The changes in the pancreas may reasonably be interpreted as the result of the obstruction of the small or large pancreatic ducts. The ducts of Wirsung and Santorini were atretic in some cases but not in others, and sometimes one was atretic while the other was normal. In case 28 (XXII) an accessory pancreas in the jejunum showed changes similar to those in the pancreas itself. The stenosis or atresia, when present, may possibly have been the result rather than the cause of the pancreatic fibrosis. It was apparent that at least in the majority of cases the smaller ducts were the primary site of the obstruction.

The time at which the obstruction occurs is important in the consideration of pathogenesis. That the lesion may be congenital is proved by the presence of extensive fibrosis of the pancreas in the 5 infants who died in the first week of life. The neonatal onset of the nutritional disturbance in the majority of cases suggests that the pancreatic lesion is usually present at birth. In case 42 (XXI), however, no abnormalities were noticed in the child until an acute infection occurred at the age of 16 months. Since the details of the early development were wanting in this case, the evidence that it presented was not weighty; but the possibility of a postnatal origin in some cases cannot be excluded.

In a high percentage of these cases there were congenital abnormalities in addition to those in the pancreas; these abnormalities were nearly all atresias or stenoses of epithelium-lined passages such as the intestine, the cystic duct or the ureters. Biliary cirrhosis in the presence of normal common and main hepatic ducts may also be interpreted as the possible result of obstruction of the smaller biliary passages. One gains the impression that there was a general tendency to atresia of ducts. If these abnormalities were omitted, few malformations would remain, and those not the exterme variety that are so often observed in cases of multiple congenital anomalies.

One must therefore consider the possible causes of an obstruction of the smaller pancreatic ducts which occurs in fetal life in association with atresia or stenosis of other epithelium-lined passages and sometimes appears in several siblings of the same family. Three etiologic agents fulfil these requirements, namely (1) congenital malformation; (2) inflammation of the pancreas during fetal life, and (3) vitamin A deficiency during fetal life.

1. The evidence in favor of the view that cystic fibrosis of the pancreas is a congenital anomaly consists of three points: The lesion was present at birth in most if not all cases; it was familial, and it was associated with other congenital anomalies. Against this is the fact that the other anomalies were for the most part atresias or stenoses in other organs, which may well have been the result of some circumstance of gestation which affected various epithelium-lined passages.

2. The presence of slight degrees of inflammation in all the cases of group I and in some of the cases of groups II and III is the most important evidence that fetal inflammation was the cause of the lesion. The general tendency to atresia can be explained on the basis of inflammation, but the familial occurrence cannot. It is possible that in the cases of obstruction of the intestine in the newborn the pancreatic changes were secondary to ascending infection. Fibrosis of the pancreas is a common finding is cases of congenital syphilis, and the question of a syphilitic infection must be considered; a fetal infection

of unknown origin is also a possible explanation. Against these arguments there stands the fact that the microscopic appearance of the pancreas in the cases of intestinal obstruction was similar to that in the cases in which the patients died in early infancy but after the neonatal period, so that it is difficult to believe that the cause was different in the two groups. It is improbable that syphilis is the cause of cystic fibrosis of the pancreas because none of the infants showed other clinical or pathologic evidences of the disease. They were born at full term with few exceptions, and the serologic tests, when made, gave negative results. Moreover, the microscopic picture of the pancreas is different with the two diseases: Fibrosis, inflammation and abnormalities of fetal structure are the predominant changes observed in cases of syphilis, whereas in cases of cystic fibrosis of the pancreas the cysts predominate, the fibrosis is less extensive and the islands of Langerhans appear normal. The possibility of a fetal infection of unknown origin cannot be gainsaid, but the evidence for it is slight. In cases with a late onset one cannot entirely discard the idea of postnatal infection as the cause of the disease. In surprisingly few of the cases was there a history of diarrhea with loose or watery stools. The few bacteriologic studies that were made gave no evidence of dysentery. Moreover, in the process of examining the 605 pancreatic sections of the last 1,000 autopsies in the Babies Hospital, many cases of diarrhea and other diseases of the intestine were encountered, and in none of them was there any evidence of pancreatitis. All cases in which there was acute inflammation of the pancreas were investigated and observed to be examples of either acute peritonitis or septicemia with mesenteric adenitis. Garsche [3n] described 2 cases of pancreatic insufficiency; in 1 the condition began in the fifth year as infectious jaundice, and in the other there was a history of chronic diarrhea with onset at the about the age of 1 year. The fibrosis of the pancreas observed post mortem in these cases differed from cystic fibrosis of the pancreas in that cysts were absent and acinar tissue was present. The author stated the belief that this represented an earlier phase of the disease noted in his third case, which is included in the present series.

3. In spite of ignorance concerning vitamin A deficiency during fetal life, this lack has been considered as a possible cause of cystic fibrosis of the pancreas because the postnatal deficiency is known to produce proliferation and metaplasia of the epithelium in various places throughout the body.[16] This hypothesis would explain the presence of atresias of other ducts as well as the regular occurrence of fibrosis of the main pancreatic ducts. The familial incidence may be the result of insufficient

16. Wolbach, S. B., and Howe, P. R.: Tissue Changes Following Deprivation of Fat-Soluble A Vitamin, J. Exper. Med. **42**:753, 1925.

vitamin A in the maternal diet or of a disturbance in the mechanism of absorption of the vitamin in the mother. In the experimental and pathologic studies of postnatal vitamin A deficiency the pancreas is found affected slightly if at all. Vitamin A deficiency in the mother's diet is known to decrease the vitamin A reserves of the young [17] and to produce a high mortality during the fetal or neonatal life.[18] No adequate anatomic studies on congenital vitamin A deficiency have been reported. The question appears capable of an experimental solution, and an investigation of the problem is at present under way in this laboratory.

PATHOLOGIC PHYSIOLOGY

Relation of the Pancreatic Lesion to the Clinical Picture.—The literature relating to the exclusion of the pancreatic juice from the intestine has recently been summarized by Ivy [19] and by Greenberg,[20] and a review will not be attempted here. Such experiments in the dog result in a clinical picture closely resembling that of cystic fibrosis of the pancreas. The similarity is sufficiently marked to confirm the belief that the syndrome in the cases presented here was due to the pancreatic lesion. The symptoms produced by ligation of the pancreatic duct or by the creation of an external fistula are hunger, polyphagia, failure to gain weight or loss of weight and bulky foul stools. Unless special care is taken, early death ensues. The animal may survive and gain in weight in the presence of a small amount of functioning pancreas, the amount necessary being estimated at 10 per cent of normal. The same result may be obtained by feeding large amounts of a well balanced diet with high vitamin content or by feeding raw pancreas.[19] These symptoms are identical with those which accompany cystic fibrosis of the pancreas; they are not found unless approximately 90 per cent of the pancreas is involved. As in the dogs, gain in weight may occur with an adequate and appropriate diet (case 44 [XX]). In both instances a large portion of the ingested food is lost in the stools, and the loss of fat is especially striking. In both cases the percentage of split fat in the stools may be

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normal.[20] A low or normal blood sugar value was found in the present cases, and a normal one has been described in experimental animals.[20] In infants the dextrose tolerance curve may be flat or high. The latter curve has been described in animals.[21] Observations on serum tributyrinase and amylase were recorded in only 1 case of cystic fibrosis of the pancreas, in which the tributyrinase content of the serum remained normal and the amylase content was high. These findings are present after experimental ligation of the pancreatic duct.[22] There is thus a close parallel between the picture presented by cystic fibrosis of the pancreas and that produced by experimental ligation of the pancreatic duct or by fistula.

The ability to split fat is found in varying degrees both in the patients observed clinically and in experimental animals, and this may be attributed to the lipase of the succus entericus. It is less easy to understand why the fatty acids are not absorbed. It most cases there are no microscopic changes in the intestine which would indicate failure to function normally, and when changes are present they are mild and may well be interpreted as the result rather than the cause of the abnormal stools. The normal mechanism of fat absorption is poorly understood, but recent work indiactes that fats are probably not absorbed as fatty acids but first undergo phosphorylation.[23] It is possible that some further step beyond the splitting of neutral fat into fatty acids is necessary in the preparation of fat for absorption and that some factor essential to this step is contributed by the pancreas.

The frequent occurrence of fatty liver in both the experimental animals and the cases collected here is another point of similarity which is not explained. The literature on the etiology of fatty liver is too vast to be reviewed here. The recent work of Dragstedt, Van Prohaska and Harms [24] may be mentioned: They have demonstrated a factor in the pancreas which is not found in pancreatic juice and which prevents fatty degeneration of the liver in pancreatectomized dogs. The application of these observations to the present problem awaits further study.

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23. Sinclair, R. G., and Smith, C.: The Turnover of Phospholipoids in the Intestinal Mucosa, J. Biol. Chem. **121**:361, 1937.

24. Van Prohaska, J.; Dragstedt, L. R., and Harms, H. P.: The Relation of Pancreatic Juice to the Fatty Infiltration and Degeneration of the Liver in the Depancreatectomized Dog, Am. J. Physiol. **117**:166, 1936. Dragstedt, L. R.; Van Prohaska, J., and Harms, H. P.: Observations on a Substance in Pancreas (a Fat-Metabolizing Hormone) Which Permits Survival and Prevents Liver Changes in Depancreatectomized Dogs, ibid. **117**:175, 1936.

Deficiency of Fat-Soluble Vitamins.—Vitamin A deficiency has been considered as a possible cause of cystic fibrosis of the pancreas; it will now be discussed as a probable result of the lesion. There was evidence of vitamin A deficiency in 10 of the 49 cases of the present series. Of the 12 reported cases of vitamin A deficiency in which postmortem examination was done, the pancreas was examined microscopically in 7, and in all 7 it was described as composed of epithelium-lined cysts and fibrous tissue. This association is too frequent to be accidental. Pancreatectomized dogs also fail to assimilate vitamin A normally.[25] Previous authors have suggested that there may be inadequate absorption of the vitamin from the alimentary tract if absorption of fat is inadequate.[26]. It is otherwise difficult to explain the fact that in several of the cases reported as instances of vitamin A deficiency the patient had received cod liver oil in amounts which were supposedly adequate (Blackfan and Wolbach's cases 3 and 7 [4a]). Two patients were given cod liver oil after admission to the hospital without beneficial effect,[27] while another recovered from xerophthalmia only after parenteral injection of carotene (case 23 [XV]). In the other cases of vitamin A deficiency the intake was probably inadequate.

The clinical tests for the determination of vitamin A deficiency have not as yet been applied in cases of cystic fibrosis of the pancreas. Studies on night blindness and on the vitamin A content of the serum have been made in cases of celiac disease.. Chesney and McCoord,[28] using the Price-Carr colorimetric method, found that the vitamin A content of the serum in 2 untreated patients with celiac disease was less than half the mean value of the vitamin in the serum of 12 controls; four hours after the administration of 2 cc. of halibut liver oil the serum of the controls showed a mean rise of approximately 900 per cent in vitamin A, whereas 1 of the patients with celiac disease showed a slight rise and the other no change. After treatment there was a rise in the basal level but not in the response to halibut liver oil. More recently Friderichsen and Edmund developed a modification of the method for determining dark adaptation which can be applied to small infants.[29] They demonstrated that a mild degree of failure in adaptation

25. Ralli, P. E.; Pariente, A.; Flaum, G., and Waterhouse, A.: A Study of Vitamin A Deficiency in Normal and Depancreatized Dogs, Am. J. Physiol. **103**:458, 1933.

26. Basu, N. K.: Vitamin A and Fat Metabolism, Ztschr. f. Vitaminforsch. **6**:106, 1937.

27. Blackfan and Wolbach.[4a] Cabot Case 17242.[4c]

28. Chesney, J., and McCoord, A. B.: Vitamin A of Serum Following Administration of Haliver Oil in Normal Children and in Chronic Steatorrhoea, Proc. Soc. Exper. Biol. & Med. **31**:887, 1934.

29. Friderichsen, C., and Edmund, C.: Studies of Hypovitaminosis A: II. A New Method for Testing the Resorption of Vitamin A from Medicaments, Am. J. Dis. Child. **53**:89 (Jan., pt. 1) 1937.

is not uncommon in infants under the age of 1 year and that it disappears one-half to one hour after feeding preparations high in vitamin A.[30] One child, aged 14 months, who presented symptoms of celiac disease, showed an especially severe degree of night blindness, which did not respond to therapy until mother's milk was given.[31] In this case and in those of Chesney and McCoord the state of the pancreas was not known. The earlier conviction that vitamin A deficiency is rare in celiac disease[32] must therefore be modified to the belief that subclinical degrees of the deficiency are not infrequent. The question deserves further investigation.

Severe vitamin A deficiency occurred in 10, or 23 per cent, of 44 cases of cystic fibrosis of the pancreas, as shown by the presence of keratinizing metaplasia of the epithelium of various organs and by xerophthalmia. Mild degrees of the deficiency may have been present in some or all of the remainder of the cases. It is not surprising that the deficiency was more marked in these cases than in those of celiac disease in patients over the age of 1 year, for the vitamin A reserves of the infant are low,[33] and there is correspondingly greater sensitivity to inadequate ingestion or absorption of the vitamin. The slow growth of these infants may be attributed in part to inadequate absorption of vitamin A.

The cause of death in all of the cases in which the patients survived the first week was bronchitis, bronchiectasis or bronchopneumonia, and this uniformity could not be accidental. The lungs of the 9 patients who showed keratinizing metaplasia of the bronchial epithelium were similar in other respects to those of the patients who did not. Mild tubular bronchiectasis with an increase in the number of cell layers in the bronchial epithelium was almost invariably observed in our series. The possibility that this was the result of a partial deficiency of vitamin A should be considered. Bronchiectasis is present in a high percentage of vitamin A-deficient rats,[16] but because of the frequency of this lesion in rats given adequate diets this species of animal is unsatisfactory for the

30. Friderichsen, C., and Edmund, C.: Studies of Hypovitaminosis A: III. Clinical Experiments in the Vitamin A Balance in Children After Various Diets, Am. J. Dis. Child. **53**:1179 (May) 1937.

31. Friderichsen, C.: Quantitative Investigations of the Resorption of A Vitamin in a Case of Coeliaki, Acta pædiat. **18**:377, 1936.

32. Parsons, L. G.: Celiac Disease; Rackford Memorial Lectures, Am. J. Dis. Child. **43**:1293 (May, pt. 2) 1932.

33. Debré, R., and Busson, A.: La vitamine A, son métabolisme, son rôle dans certains états pathologiques chez l'homme, Rev. franç. de pédiat. **10**:413, 1934. Wolff, L. K.: On the Quantity of Vitamin A Present in the Human Liver, Lancet **2**:617, 1932.

experiment.[34] Similar investigations on other species would be of greater interest.

The evidence for vitamin D deficiency is less clear. Severe rickets was described in only 1 case,[3k] but osteoporosis was often mentioned and was present in most of the cases of the Babies Hospital. This may be interpreted either as the result of failure of calcium absorption due to the fixation of the ingested calcium by the fatty acid in the intestine to form soaps, or as the result of vitamin D deficiency. The absence of rickets is not surprising in view of the slow growth of these children.

Deficiency of the Water-Soluble Vitamins.—No evidence of deficiency of water-soluble vitamins was recognized.

RELATION TO CELIAC DISEASE

In most of the cases of the present series in which the patients survived the first six months of life the clinical diagnosis was celiac disease; this diagnosis was based on the presence of most if not all of the characteristics of the celiac syndrome. The traditional points of differentiation between idiopathic and pancreatic steatorrhea, namely, the character of the stools and the failure of the latter condition to respond to a diet for patients with celiac disease, have been shown to be unreliable. At present the differential diagnosis can be made with certainty only by examination of the duodenal juice for pancreatic enzymes or by microscopic examination of the pancreas. In most of the reported cases of celiac disease neither of these tests was applied, and the reader is therefore uncertain as to whether the pancreas was normal or not. The literature has accordingly been searched for cases of celiac disease in which autopsy was done, and 32 of them have been found, exclusive of those in which cystic fibrosis of the pancreas or replacement of the acinar tissue with fat occurred. In the reports of 17 of them there was no definite statement that the pancreas was examined microscopically, namely, in the cases of Moorehead,[35] Pipping,[36] Bloch,[37] Schick and Wagner,[38] and Baginsky [39] and in 1 case of Passini,[3c] 1 of Miller,[40]

34. Passey, R. D.; Leese, A., and Knox, J. C.: Bronchiectasis and Metabolism in the Lung of the Laboratory Rat, J. Path. & Bact. **42**:425, 1936.

35. Moorehead, T. G.: Infantilism, Pancreatic and Intestinal, Dublin J. M. Sc. **149**:1, 1920.

36. Pipping, W.: Beitrag zur Kenntnis des intestinalen Infantilismus (Herter), Acta pædiat. **3**:342, 1924.

37. Bloch, C. E.: Clinical and Anatomical Investigations of Infantilismus, Acta pædiat. (supp. 2) **7**:207, 1928.

38. Schick, B., and Wagner, R.: Ueber eine Verdauungsstörung jenseits des Säuglingsalters (Atrophia pluriglandularis digestiva), Ztschr. f. Kinderh. **35**: 263, 1923.

(Footnotes continued on next page)

all but 2 of Fanconi's 6 cases [41] and 3 of the 6 cases of nontropical sprue collected by Thaysen.[42] In the remaining 15 cases the microscopic examination of the pancreas revealed no extreme changes. Four of these were cases of nontropical sprue or celiac disease beginning in adult life.[43] Since this disease is irrelevant to the present investigation, these cases will not be discussed. There remain 11 cases of celiac disease beginning in infancy or early childhood in which the pancreas was examined microscopically and was observed to show no extreme changes (Mautner,[44] Porter,[45] Hess and Saphir's case 3,[31] Fanconi's cases 34 and 40,[41] Poynton and Paterson,[46] Miller,[47] Kundratitz,[48] Still,[49] Poynton, Armstrong and Nabarro [50] and Fullerton and Innes [51]).

39. Baginsky, A.: Die wichtigsten Verdauungsstörungen des älteren Kindes und ihre Behandlung, Arch. f. Kinderh. **64**:161, 1915.

40. Miller, R.: The Pathogenesis of Celiac Disease, Arch. Pediat. **40**:88, 1923.

41. Fanconi, G.: Der intestinale Infantilismus und ähnliche Formen der chronischen Verdauungsstörung, Abhandl. a d. Kinderh. u. Grenzgebieten (supp. to Jahrb. f. Kinderh.) **21**:1, 1928.

42. Thaysen, T. E. H.: Non-Tropical Sprue: A Study in Idiopathic Steatorrhoea, Copenhagen, Levin & Munksgaard, 1932.

43. Thaysen.[42] Anderson, A. G., and Lyall, A.: Two Cases of "Fatty Diarrhoea" with Special Reference to Nitrogen Metabolism, Quart. J. Med. **2**:339, 1933. Holst, J. E.: Ein in Dänemark aufgetretener Fall von Sprue, Acta med. Scandinav. **66**: 74, 1927. Rosendahl, G., cited by Thaysen.[42] Gloor, H. U.: Klinische Erfahrungen über die Behandlung der perniziösen Anämie, Folia haemat. **39**:373, 1930.

44. There is some doubt as to whether the pancreas in Mautner's case (Mautner, H.: Die Herter-Heubnersche Verdauungsinsuffizienz [Coeliac Disease], Klin. Wchnschr. **4**:165, 1925. Lehndorff, H., and Mautner, H.: Die Coeliake, Herters intestinaler Infantilismus, Heubners schwere Verdauungsinsuffizienz jenseits des Säuglingsalter, Ergebn. d. inn. Med. u. Kinderh. **31**:456, 1927) showed cystic fibrosis. The pathologic description and the neonatal onset are in favor of this view. However, the illustration (1927) shows only fat droplets in the acinar cells, and as this evidence is objective the case has been placed in the group of those in which there was no cystic fibrosis.

45. Porter, L.: Pancreatic Insufficiency, Am. J. Dis. Child. **6**:65 (Aug.) 1913.

46. Poynton, F. J., and Paterson, H.: The Occurrence of Ascites of a Non-tuberculous Origin in Chronic Recurrent Diarrhoea in Childhood, Lancet **1**:1533, 1914.

47. Miller, R.: A Fatal Case of Coeliac Infantilism with Comments on the Morbid Anatomy of Coeliac Disease, Lancet **1**:743, 1921.

48. Kundratitz, K.: Zur Pathogenese des Herterschen intestinal Infantilismus (Heubners chronische Verdauungsinsuffizienz, Schick und Wagners Atrophia pluriglandularis digestiva, Lehndorf und Mautners Coeliakie, Coeliac Disease der english-amerikanischen Autoren), Jahrb. f. Kinderh. **116**:310, 1927.

49. Still, G. F.: The Lumleian Lectures on Coeliac Disease, Lancet **2**:193, 1918.

50. Poynton, F. J.; Armstrong, R. R., and Nabarro, D. N.: A Contribution to the Study of a Group of Cases of Chronic Recurrent Diarrhoea of Childhood, Brit. J. Child. Dis. **11**:145, 1914.

51. Fullerton, H. W., and Innes, J. A.: Case of Idiopathic Steatorrhoea with Multiple Nutritional Deficiencies, Lancet **2**:790, 1936.

TABLE 2.—*Summary of Cases of Celiac Disease With Autopsy in Which the Pancreas Showed no Marked Changes on Microscopic Examination*

Case	Author	Age at Onset of Digestive Disturbance	Age at Death	Sex	Predominant Clinical Symptoms	Cause of Death (Clinical)	Postmortem Observations	
							Data on Pancreas	Other Data
1	Mautner, 1925.....	Neonatal	2-3 yr.	M	Poor development; fatty stools; large abdomen; anemia	Acute lobar pneumonia empyema	Slight fibrosis with infiltration; fat in acinar cells	Fatty liver
2	Porter, 1913.....	4 months	3 yr.	M	Failure to gain; protuberant abdomen; vomiting; scurvy; large foul greasy stools with mucus; anorexia	Diarrhea; exhausiton	Slight fibrosis; acinar tissue normal; many islands	Emaciation; slight interstitial nephritis; intestines normal
3	Hess and Saphir, 1935, case 3	Before 4 mo.	3 yr.	F	Recurrent attacks of diarrhea; underdevelopment	Dehydration bronchopneumonia	Slight fibrosis and infiltration; acinar cells small, sometimes forming syncytium; islands normal	Emaciation; infiltration of intestinal mucosa; nephrolithiasis; fatty liver; multiple diverticula of stomach
4	Fanconi, 1928, case 40	1¾ years	3¼ yr.	?	Recurrent diarrhea; thin stools with mucus; multiple hemorrhages	Diarrhea	Acini normal; fat in island cells	Osteoporosis; multiple hemorrhages; fatty liver
5	Poynton and Paterson, 1914	1 year	3½ yr.	M	Infantile cholera; marasmus; polydipsia	Cachexia; anasarca and ascites	Small circumscribed areas of leukocytic infiltration between acini; no fibrosis	Fatty liver; edema and leukocytic infiltration of intestines
6	Miller, 1921.....	2 months	5½ yr.	M	Recurrent diarrhea; large abdomen	Acute intestinal disorder	Normal	Emaciation
7	Kundratitz, 1927.....	1½ years	6 yr. 2 mo.	F	Recurrent diarrhea; stools various, some with high fat content	Diarrhea; exhaustion	Normal	Fatty liver; stomach and intestines normal
8	Still, 1918.....	6¾ years	7 yr.	M	Loose bowels; wasting; large abdomen	Diarrhea; exhaustion	Some excess of fibrous tissue, especially around the ducts, the appearance being suggestive of some pancreatitis	Slight ascites; intestines thick, with swollen and congested mucosa; no ulcers
9	Fanconi, 1928, case 34	?	8½ yr.	F	Alternating constipation and diarrhea; stools thin, mucoid or fatty; bleeding; vomiting	Erysipelas	Fat in acinar cells, otherwise normal	Erysipelas; osteoporosis; fatty liver; fat in myocardium; anemia; hemosiderosis of spleen
10	Poynton, Armstrong and Nabarro, 1914	1 year	9 yr.	M	Recurrent diarrhea; large foul stools	Diarrhea; exhaustion	Marked fibrosis of interlobular tissue; gland tissue normal	Acute congestion and lymphoid infiltration of stomach and intestines (Bacillus of Flexner); fatty liver
11	Fullerton and Innes, 1936	Early infancy	33 yr.	F	Recurrent diarrhea; fatty stools; vitamin deficiencies (B_2, D, antianemic)	Septicemia (streptococcus)	Relative increase in islands, otherwise normal	Streptococcic septicemia; peritonitis; hydrothorax; fatty liver

A comparison of the records of this group with the cases collected for the present paper shows several points of difference in the clinical course (tables 1 and 2). In the former group the first gastrointestinal symptoms were noted between the ages of 2 months and 1 year in 5 cases and between the first and the seventh year in 4 cases; the age of the child at occurrence of these symptoms was not stated in the reports of the remaining 2, but it was before the eighth year. The first part of the illness consisted in recurrent attacks of diarrhea, the stools varying in different cases and at different times in the same case but in general changing gradually from a watery, greenish type in the early part of the course to a large, foul, pale type later. Underdevelopment and failure to gain weight were mentioned frequently. Death followed a recurrence of acute diarrhea in 6 cases; of the remaining cases the terminal event was erysipelas in 1, streptococcic septicemia in 1 and infection of the respiratory tract in 2; it was not stated in the report of 1 case. There was evidence of scurvy in 1 case [45] and possibly in another.[41]. In the case of Fullerton and Innes [51] the patient showed multiple vitamin deficiencies (B_2, D, antianemic factor). Death occurred in the majority of cases between the third and the ninth year, but 1 patient survived to the thirty-third year. In 2 cases the pancreas was entirely normal, and in the others, it showed mild changes, which consisted of mild fibrosis in 6 cases and slight cellular infiltration in 1 case. The acinar tissue was normal in 9 cases and contained fat in 1; in another the acinar cells were arranged as syncytium. The changes observed in the other cases were too various to be enumerated in detail. The liver was fatty in 8 cases; the intestines were normal in most instances but contained an excess of lymphocytes in the mucosa in 4. The striking points in the cases of this group which differentiated them from those in which there was cystic fibrosis of the pancreas are (1) the later age of onset; (2) a period of recurrent attacks of diarrhea preceding the appearance of fatty stools, in most of the cases without severe pancreatic change; (3) absence of hunger and polyphagia; (4) a longer survival; (5) absence of evidences of vitamin A deficiency, and (6) death as the result of an exacerbation of the diarrhea, though sometimes an intercurrent infection was responsible, whereas in the cases of pancreatic disease death was due to infection of the respiratory tract.

The cases in which there were no striking pancreatic changes do not present as uniform a picture as those in which there were pancreatic changes and possibly do not represent a disease entity. Most if not all of them can be interpreted as cases of recurrent diarrhea of unknown cause with fatty diarrhea in the latter part of the course. Whether the diarrhea was due to a single cause is unknown, and bacteriologic studies have yielded no satisfactory conclusions. A probable

cause was demonstrated in only 1 of these cases as the Flexner bacillus, but this may have been a secondary invader. It appears probable that the cases of celiac disease in which the course terminated in recovery belong to the group in which the pancreas was essentially normal, since in the recorded cases of cystic fibrosis of the pancreas the oldest patient died before the fifteenth year.

The clinical picture of celiac disease, with retarded development, muscular weakness and atrophy, a large abdomen, large foul stools and a favorable response to the standard regimen for this condition, is found in cases of chronic recurrent diarrhea in which the pancreas is normal and also in cases of cystic fibrosis of the pancreas. Celiac disease may therefore be regarded as a clinical syndrome rather than a disease entity. Cystic fibrosis of the pancreas is a disease entity which produces the celiac syndrome when the children survive the first year of life. The remaining cases of celiac disease, including most if not all of those in which recovery occurs, form a group which is less uniform and which may represent one or more disease entities. At present the differential diagnosis can be made with certainty only by examination of the duodenal contents for pancreatic enzymes or by microscopic examination of the pancreas.

THERAPY

As yet too little is known of cystic fibrosis of the pancreas to warrant a detailed account of treatment. There are, however, several indications which should be recorded. 1. The children who survived the first few months of life are those who received mother's milk with the addition of cod liver oil or other preparations of the same order and who were later given a diet for celiac disease. 2. The frequency of vitamin A deficiency suggests that large doses of fat-soluble vitamins should be given. In some cases it may be advisable to give them parenterally. A diet low in fat appears to produce improvement in the stools, but the hazard of vitamin A deficiency and of pulmonary infection is so great that it seems unsafe to use it; fatty stools are preferable to fatal purulent bronchitis. 3. Experiments on ligation of the pancreatic duct in dogs have demonstrated that the animals require a greater quantity of food than normal to maintain health. The absolute amount of food which is absorbed increases with the amount ingested, although the proportion decreases.[19] It is suggested that this observation be applied in the cases of pancreatic insufficiency and that the caloric intake be in excess of the usual amount for the age.

SUMMARY AND CONCLUSIONS

Forty-nine cases of pancreatic fibrosis in infants or older children on whom postmortem examination was done have been collected and

analyzed. Forty-five of these were cases of cystic fibrosis of the pancreas and 4 were cases in which the acinar tissue of the pancreas was replaced by adipose tissue.

Clinically the cases fell into three groups, as follows:

1. In 5 cases death occurred in the first week of life, from some form of intestinal obstruction.

2. In 19 cases of infants the patients died between the ages of 1 week and 6 months, of purulent bronchitis, bronchiectasis or bronchopneumonia. In 13 of these cases the patients presented feeding problems, the essential features of which were hunger, failure to gain on an adequate diet in the absence of vomiting or diarrhea, and the presence of foul bulky stools.

3. In 25 cases the children died of pulmonary infections between the ages of 6 months and 14½ years. All these patients presented symptoms which were recognized as preceliac in type or which led to the diagnosis of celiac disease.

The chief pathologic changes were as follows:

1. The acinar tissue of the pancreas was replaced by epithelium-lined cysts containing concretions and surrounded by fibrous tissue. The islands of Langerhans were intact.

2. The lungs showed bronchitis, bronchiectasis, pulmonary abscesses arising in the bronchi, lobular pneumonia or any combination of these. Staph. aureus was the usual bacteriologic agent.

3. There was evidence of vitamin A deficiency in many of the patients who died before the age of 1 year.

4. Atresia of the small intestine, of the cystic duct or of the pancreatic duct was frequently noted.

The cause of the pancreatic lesion was unknown. In all probability it was usually if not always present at birth. Sixty-seven per cent of the patients were girls. There were 3 proved instances of familial occurrence. The racial and geographic distribution was wide. Cystic fibrosis involved 90 per cent (estimated) of the pancreatic tissue in 3.3 per cent of 605 unselected cases in which autopsy was done in the Babies Hospital.

The relation of the pancreatic lesion to the other clinical and pathologic observations has been discussed:

1. The clinical syndrome was comparable to that which follows ligation of the pancreatic duct in dogs; it can be attributed to the pancreatic lesion. Under favorable circumstances the symptoms of the condition sometimes disappeared temporarily (for a period of several months) under the influence of appropriate dietary treatment.

2. The frequent occurrence of vitamin A deficiency was probably due to failure of absorption of this vitamin. It is suggested that the pulmonary infection was possibly secondary to vitamin A deficiency.

3. Osteoporosis was frequent and can be interpreted as the result of inadequate absorption of either vitamin D or calcium or both.

4. The fatty degeneration of the liver and the occasional lymphocytic infiltration of the intestinal mucosa are considered secondary.

Thirty-two further cases of celiac disease in which postmortem examination was done have been collected from the literature. In 11 of these, the disease began in childhood and the pancreas was examined microscopically. No marked changes were observed in the pancreas. The clinical and pathologic observations in these cases have been compared with those in the cases of pancreatic insufficiency. The former group is less homogeneous, but the disease usually began as chronic recurrent diarrhea of unknown origin, with fatty stools in the latter part of the course. Onset and death were later than in cases of pancreatic insufficiency.

The clinical picture of celiac disease may be presented either by patients with pancreatic insufficiency who survive the first year of life or by patients with chronic recurrent diarrhea who have no essential abnormalities in the pancreas. The two groups of cases can be differentiated with certainty only by examination of the duodenal contents for enzymes or by microscopic examination of the pancreas. It is concluded that celiac disease is a clinical syndrome, not a disease entity, and that it may be produced by two or more disease entities, one of which is cystic fibrosis of the pancreas.

CASE 7 (IV).—A. L. was a girl. The parents were well. One sibling died at the age of 3 months, having had diarrhea and having failed to gain. The birth was normal and occurred at term. The weight at birth was 8½ pounds (3,856 Gm.). The child was nursed until the eighth day, when she was given similac "because the mother's milk had Staph. albus." The child had boils on the arms. At this time the weather was extremely hot and she failed to take her formula well. The stools were green and foul but numbered not more than 4 a day. The child had several cyanotic attacks. She was admitted to the Babies Hospital at the age of 6 weeks, the complaint being failure to gain weight.

Physical Examination.—The weight was 7½ pounds (3,402 Gm.), the length 55 cm. and the temperature 99.6 F. The patient was well developed and thin, with a vigorous cry. There was a small umbilical hernia. The ear drums were a little red, the right more so. Otherwise the examination gave negative results.

Laboratory Findings.—The hemoglobin content was 23 Gm. per hundred cubic centimeters. The red cell count was 5,600,000, and the white cell count 26,000. There were 63 per cent polymorphonuclears. The urine was normal except for a trace of albumin. The Kahn reaction was negative. There were 2 to 5 stools daily; these were large, foul, soft and yellow or green.

Course.—During the first part of her stay the infant took feedings well and appeared hungry. There was a small gain in weight. After a week the temperature rose to 101 or 102 F. and the respiratory rate to 60. The patient lost a little weight and began to cough. The subsequent course was that of pneumonia. The child died fifteen days after admission.

Autopsy.—The age at death was 8 weeks, the weight 7 pounds (3,175 Gm.) and the length 57 cm.

Gross Examination: The peritoneal cavity appeared normal except for distention of the small and especially of the large intestine.

The lungs bore a yellowish gray fibrinous exudate. The surfaces were studded with abscesses measuring 2 to 10 mm. in diameter. The intervening lung tissue was purplish red. The cut surface was honeycombed with small anastomosing cavities which appeared to be infected dilated bronchi. A probe was passed from the larger ones directly into the bronchi. The hilar lymph glands were large, gray and moist.

The liver weighed 240 Gm. It had a brownish tinge but otherwise appeared normal.

The pancreas was normal externally and on section.

The right middle ear was normal. The left middle ear and mastoid antrum contained a thick purulent exudate.

The remaining viscera showed no significant gross changes.

Bacteriologic Examination: This showed Staph. aureus haemolyticus in material from the left middle ear and in the pleural exudate.

Microscopic Examination: The bronchi and bronchioles were filled with purulent exudate. The walls of the bronchioles were infiltrated with lymphocytes, myeloid cells and an occasional polymorphonuclear leukocyte. Several large abscesses containing numerous bacteria were present. Many of the intervening alveoli contained coagulated fluid, but the walls were free from exudate. Gram's stain showed that many bacteria, morphologically classed as staphylococci, were present in the abscesses and in the exudate in the alveoli and bronchi and on the pleural surface.

Some of the cells of the liver contained fat vacuoles. Brown pigment was present in both hepatic and Kupffer cells. The iron stain showed that iron-containing pigment was abundant in the hepatic cells and in the Kupffer cells.

In nearly all the lobules of the pancreas, the ducts were mildly to widely dilated and the lumens contained pale vacuolated mononuclear cells or laminated hyaline concretions. The islands were intact. Fibrous tissue containing many fibroblasts separated the acini as well as the lobules. Small numbers of lymphocytes and mononuclear cells and a few eosinophils were seen in this fibrous tissue (fig. 7).

The other organs appeared normal.

Anatomic Diagnosis: The diagnosis was purulent bronchitis; lobular pneumonia with abscess formation (Staph. aureus haemolyticus); acute fibrinous pleurisy (Staph. aureus haemolyticus); purulent otitis media (Staph. aureus haemolyticus); cystic fibrosis of pancreas, and accidental involution of the thymus.

Case 9 (V).—M. A. was a girl. The parents and one older sibling were living and well. The patient was the result of the second pregnancy. The birth was normal. The weight at birth was 5 pounds and 10 ounces (2,251 Gm.). The child never took the breast well and was given a supplementary formula containing cow's milk and dextrimaltose with ½ teaspoon of cod liver oil. The appetite was good for the bottle but not for the breast feeding. There were 2 or 3 regular

bowel movements a day. Two weeks before admission to the hospital the baby began to cough. Two days before admission the cough became more frequent and spasmodic, and the coughing spells were followed by dyspnea and on two occasions by vomiting. The appetite decreased. The temperature was normal.

Physical Examination at Two Months.—The temperature was 99.4 F., the weight 7 pounds and 2 ounces (3,232 Gm.) and the length 53 cm. The child appeared small but well. The skin was sallow, with marked hypertrichosis. The pharynx was mildly injected. There was a frequent spasmodic, high-pitched, choking cough. Respirations were rapid and shallow, with moderate retraction of the lower costal margins and of the suprasternal notch. There were a few moist rales at the bases of both lungs.

Laboratory Findings.—The hemoglobin content was 11 Gm. per hundred cubic centimeters. There were 4,340,000 red cells and 13,450 white cells per cubic millimeter, of which polymorphonuclears constituted 41 per cent, lymphocytes 56 per cent, mononuclears 2 per cent and eosinophils 1 per cent. The urine was normal. Culture of material from the throat showed Staph. albus nonhaemolyticus and Staph. aureus haemolyticus. Blood cultures were negative. Roentgenograms of the heart showed bilateral bronchopneumonia, more marked on the left.

Course.—The child was thought to have pertussis or capillary bronchitis. Her condition rapidly became worse, and she died at the age of 2½ months, twelve days after admission to the hospital.

Autopsy.—The age at death was 2½ months, the weight 3.3 Kg. and the length 54 cm.

Gross Examination: The child was small but fairly well nourished. There was a mucopurulent discharge in both nostrils. The abdomen was prominent, with slight protrusion of the umbilicus. The peritoneum contained 3 cc. of clear fluid. The arch of the aorta lay below and somewhat to the left of the normal position, so that the superior surface was at the level of the bifurcation of the trachea. The right subclavian artery arose below the left subclavian artery and followed an anomalous course; it passed behind the trachea and esophagus, going diagonally upward and laterally along the posterior wall of the right chest to pass over the first rib at the usual point.

The heart was normal except for some dilatation of the right ventricle.

The right lung weighed 65 Gm. The pleura was smooth. The posterior half of the lung was firm and nodular, with dilatation of the interlobular lymphatics. The anterior portion was emphysematous, with patches of atelectasis. The cut surface was firm, moist and salmon pink, with gray areas around the bronchi. All the bronchi and bronchioles appeared a little enlarged and thickened, with a thick white exudate in the lumens. The left lung weighed 60 Gm. It resembled the right.

The spleen weighed 10.5 Gm. It was pale red, with indistinct malpighian corpuscles. An accessory spleen 1 cm. in diameter lay near the hilus.

The liver weighed 135 Gm.; it appeared normal except for a yellowish tinge. The gallbladder was atrophic and contained 1 or 2 cc. of thick gray translucent mucoid material. The cystic duct was not patent, but the hepatic and the common duct were normal.

The pancreas was of almost normal size and had a pinkish tinge. On section the lobules were irregular in size, rounded and often fused together. Wirsung's duct could not be demonstrated. The duct of Santorini was present and patent, though small. The pancreatic tissue around it was similar to that seen elsewhere.

The left kidney weighed 15 Gm. There was mild hydronephrosis, but the cortex appeared normal otherwise. There were three areas of stricture, one at the ureteropelvic junction and the others just below. The circumference was 1 mm. at the narrowest point and 4 mm. below the strictures. The right kidney weighed 14 Gm. and appeared normal. There was a slight narrowing of the uteropelvic junction but no dilatation of the kidney pelvis.

The adrenals, alimentary tract and cervical organs were normal.

Microscopic Examination: The bronchi and bronchioles were dilated and filled with an exudate of polymorphonuclear leukocytes, cellular débris and bacteria. The bronchial epithelium was intact for the most part. There were occasional areas where the epithelium was pseudostratified, but no areas of squamous metaplasia were noted. Near the bronchioles the alveolar walls were thickened, and some of the alveoli were filled with polymorphonuclear leukocytes, red cells and lymphocytes. The less affected alveoli were emphysematous. The Gram stain showed many gram-positive cocci in the cellular débris in the bronchial lumens.

The malpighian corpuscles of the spleen were small and surrounded by red cells and polymorphonuclear leukocytes. The pulp contained eosinophils, normoblasts and phagocytes in which was brown pigment. The iron stain showed that a moderate amount of iron was present within phagocytes.

The hepatic cells contained fat vacuoles and granules of hemosiderin. A few lymphocytes and myelocytes were found in the portal areas.

In the mucosa of the gallbladder there were many epithelium-lined cysts containing mucus. Both the common and the cystic duct contained small epithelium-lined cysts full of mucus.

The acini of the pancreas varied in size, ranging from small and atrophic structures to large cysts. Many of them contained eosinophilic material and were lined by more or less flattened epithelium. There was a moderate increase in interstitial tissue, which was infiltrated with plasma cells and lymphocytes. An occasional polymorphonuclear leukocyte was present. The islands of Langerhans were normal.

There were occasional areas of pseudostratification in the mucosa of the fundus of the uterus.

The cortex of the thymus was depleted of small cells. Many eosinophils and myelocytes were present.

The adrenal glands, kidneys, intestines, thyroid and vagina appeared normal.

Bacteriologic Report: The lungs contained Staph. aureus haemolyticus. No growth occurred in material from the peritoneum.

Anatomic Diagnosis: The diagnosis was cystic fibrosis of the pancreas; bronchiectasis; acute bronchitis; lobular pneumonia; acute splenic tumor; atresia of the cystic duct; cysts of the cystic duct and of the gallbladder; congenital malformation of the ureters (strictures of ureters at and below the ureteropelvic junction); hydronephrosis on the right, and congenital malformation of the aorta (anomalous origin and course of the right subclavian artery).

Case 23 (XV).—M. D. was a boy. The parents were well. One older sibling died of cystic fibrosis of the pancreas and bronchopneumonia at the age of 9 months at the Mount Sinai Hospital, and her case is included in this report (case 28 [XXII]). There were no other pregnancies.

The child was born in Sloane Hospital after a normal pregnancy. He appeared normal at birth. The weight at birth was 7 pounds and 11 ounces (3,487 Gm.). The infant received breast milk and a complementary formula of evaporated milk

and dextrimaltose. A little blood was found in the stools, but there was no known infection. After birth the child's weight fell to 6 pounds and 5 ounces (2,863 Gm.) but it had increased to 6 pounds and 12 ounces (3,062 Gm.) on discharge from the hospital on the nineteenth day. At that time the patient was having 6 or 7 loose stools a day, which contained blood, mucus and curds.

During the subsequent three and one-half months the infant did not do well, and a great many formulas were tried. Cod liver oil was first given at 8 weeks, but this "went right through the child," increasing the number of stools. The boy received outdoor sunshine. An "iron solution" and orange juice increased the number of stools. Transfusions produced some improvement. At 3 months the child weighed 10 pounds and 5 ounces (4,678 Gm.), but he then lost weight and was thought to have heat prostration. At 4 months roentgenograms of the chest and abdomen appeared normal. At this time the infant was put on a formula containing goat's milk and banana powder, which produced improvement in his general condition and reduced the stools to 2 a day. At 4½ months his temperature rose to 103 F., and leukocytes were found in the urine.

Beginning at the third month, there was a discharge in the right conjunctival sac, which improved on local treatment. A week later an ulcer appeared in the left cornea, and a diagnosis of xerophthalmia was made. The child was given carotene by mouth and also in the left eye, with healing of the ulcer but an increase in the number of stools. The child ate well and vomited only occasionally. The infant was admitted to the hospital at the age of 4½ months with a temperature of 104.8 F.

Physical Examination.—The infant was weak, dehydrated and poorly nourished, weighing 10 pounds (4,536 Gm.). Both scleras were hazy and slightly thickened. There was a small ulcer in the upper medial portion of the left cornea. There was no photophobia; the fundi appeared normal. The pupils reacted slightly to light. The ears, nose and mouth appeared normal. There was slight enlargement of the costochondral junctions. The heart and lungs were normal. The abdomen was scaphoid and soft, with prominent intestinal loops. The liver extended 3 cm. below the costal margin, and the spleen was palpable.

Laboratory Examination.—The hemoglobin content was 9.2 Gm. per hundred cubic centimeters; there were 2,300,000 red cells and 36,100 white cells per cubic millimeter, with polymorphonuclears 74 per cent, lymphocytes 22 per cent and eosinophils 3 per cent. After several transfusions the hemoglobin content was 18.4 Gm. and the red cell count 5,000,000. The urine was cloudy; the specific gravity was 1.012; analysis showed a heavy trace of albumin, no sugar, no acetone, benzidine (3 plus), many white cells and bacteria and a few red cells. Cultures of the urine produced an organism of the paratyphoid group which did not agglutinate with stock serums against Bacillus paratyphosus A, B or C, Bacillus enteritidis or Bacillus aertrycke. The blood showed no agglutinins for stock cultures of various members of the paratyphoid and dysentery groups. The chest and abdomen appeared normal on roentgen examination except for distention of the colon. Intravenous urography gave normal findings.

Course.—The child was given several transfusions and large amounts of vitamins A, B_1 and D both by mouth and by injection. He was given a formula containing evaporated goat's milk and banana powder. There was a dry cough. The stools numbered 2 to 4 a day and varied in character. Many were soft, large and yellow. The patient was given mandelic acid, but this was discontinued as he became lethargic and acidotic. He was discharged after two weeks in the

hospital with improvement in the eyes and in the urine but without change in the general condition. After discharge the cough became worse, and the weight decreased to 9 pounds and 1 ounce (4,111 Gm.). There were two further admissions. The course was essentially one of progressive bronchopneumonia and bronchiectasis, terminating fatally at the age of 6 months.

Autopsy.—The age at death was 6 months and the weight 3.61 Kg.

Gross Examination: The body was that of an emaciated white infant. The head was somewhat square, with moderately prominent frontal bosses. There was extreme pallor of the conjunctivas and mucous membranes. The corneas were normal. The ears and mouth appeared normal. The nose exuded a thin fluid. In both cheeks there were prominences at the sites of the parotid glands, which were large, firm and freely movable and measured about 3 by 3 by 0.5 cm. The submaxillary glands were also large and firm. The salivary glands could not be removed because of restrictions on the incision. The thorax was symmetric, with a wide costal angle and slightly flaring ribs. There was slight prominence of the costochondral junctions. The abdomen was moderately rounded. The extremities were pale and thin, and there was marked muscular atrophy throughout the body. The peritoneal cavity appeared normal. The liver extended 5 cm. below the xiphoid, and the diaphragm lay at the level of the fourth rib on the right and the fifth on the left. The intestines, especially the ileum, were moderately distended. No abnormalities were found in the pleural and pericardial cavities.

The heart weighed 32 Gm. The pericardium and valves appeared normal. The myocardium was pale, soft and somewhat flabby. The foramen ovale was closed.

The right lung weighed 90 Gm. There were a few strands of fibrin over the posterior surface of the lower lobe. On palpation the lower lobe was coarsely nodular, the nodules measuring up to 2 cm. It was purplish red, with a pale network of dilated lymphatics. On section the lower lobe contained many small irregular cavities, measuring 1 to 5 mm. in diameter, which contained pus and communicated with the small bronchi. There were firm yellowish areas of consolidation around these centers. There were similar bronchiectatic cavities in the lower portion of the upper lobe. The left lung resembled the right.

The spleen weighed 17 Gm. The contours were normal. The cut surface was firm and bright red, with small malpighian corpuscles.

The liver weighed 185 Gm. It was normal in shape, with a smooth, pale red surface mottled with yellowish areas. The lobular markings were indistinct but normal in pattern.

The pancreas appeared normal in size and consistency. On section the lobules were rounded. An attempt was made to dissect out the pancreatic duct, but this was not identified.

The adrenals were small, with a thin cortex containing no lipoid.

Each kidney weighed 27 Gm. The capsules stripped with some difficulty, leaving a pale, slightly granular surface with dilated stellate venules. The cut surface was pale. The pelves and ureters appeared normal in contour but bore a reddish and granular mucosa.

The lower portion of the esophagus was somewhat dilated, and the mucosa was thickened and granular. The stomach, duodenum, jejunum and appendix were normal. There were some dilatation and hypertrophy of the terminal portion of the ilium and of the colon.

The organs of the neck, the brain and the spinal cord were not removed because of restrictions on the autopsy. The other organs appeared normal.

Microscopic Examination: The myocardium appeared normal. There was serous atrophy of the subepicardial fat.

The abscess cavities of the lung were observed to have originated as bronchiectatic cavities. In some areas their walls were formed of granulation tissue; in other places they were lined by a layer of epithelium 2 to 6 cells in thickness. There were a few areas of squamous metaplasia. The lumens of the cavities contained débris, purulent material, bacteria and, in a few places, phagocytes full of large fat vacuoles. There were also abscesses in the lung parenchyma and areas of fresh lobular pneumonia. The Gram stain showed that the bacteria in the abscesses were gram-positive cocci in clumps; morphologically they resembled staphylococci.

The epithelium of the trachea was about 4 to 6 cells in thickness. There were numerous bacteria on the surface. The ducts of some of the mucous glands showed a tendency to squamous metaplasia. The mucosa bore an ulcer beneath which there was an infiltration of polymorphonuclear leukocytes and lymphocytes.

The malpighian corpuscles of the spleen were small but normal in number. Around them were collars of red cells, among which were a few polymorphonuclear leukocytes and phagocytes. The pulp was congested; in it were a few nests of red cells and phagocytes containing hemosiderin.

The liver was normal except for small amounts of hemosiderin in the liver cells and large amounts in the Kupffer cells.

In one section of the pancreas only occasional acini appeared normal. The majority formed cysts lined with flat or cuboidal epithelium containing granular eosinophilic material and concretions. The latter were composed of concentric rings of deeply eosinophilic material and resembled corpora amylacea. Some of the cysts were irregular in shape. There was a definite increase in the connective tissue between the alveoli and also in that between the lobules. The lobules therefore varied greatly in size, and in many cases they were fused together. The islands of Langerhans appeared normal in number and in appearance. Another section was similar to the first. Small numbers of lymphocytes and plasma cells infiltrated the interstitial tissue.

Study of the kidney revealed small areas of interstitial infiltration with plasma cells and mononuclear phagocytes. There were a few gram-positive cocci and minute gram-negative cocci in the infiltrated areas.

The submucosa of the jejunum showed a slight increase in connective tissue, but otherwise the tissue was normal.

In the mucosa of the ileum there was some increase in the number of plasma cells and lymphocytes. Otherwise the tissue was similar to that of the jejunum.

Bacteriologic Examination: The material from the left lung showed Staph. aureus, slightly hemolytic.

Anatomic Diagnosis: The diagnosis was cystic fibrosis of the pancreas; avitaminosis A (clinical); bronchiectasis with abscess formation due to Staph. aureus; lobular pneumonia; lipoid pneumonia (mild); acute fibrinous pleurisy; interstitial nephritis; acute splenic tumor, and hemosiderosis of the liver and spleen.

Case 37 (XVIII).—C. H., a girl, was admitted to the hospital at the age of 8 months with the diagnosis of early celiac disease. The parents and two older siblings were living and well. The mother had spent seven months in a tuberculosis sanatorium four years earlier but had been well afterward. The patient was the result of the third pregnancy. There was no familial history of intestinal disease such as the patient's, but the mother had a sister who died at the age of 9 months of "carcinoma of the liver." The birth was normal; the weight at birth was 7

pounds and 12 ounces (3,515 Gm.). The child was never fed from the breast because the mother had had abscesses of the breast with the first baby. For the first three months the infant received a formula which contained cow's milk and Karo. There were large foul stools before the age of 2 weeks, while the child was still in the hospital. They were grayish and yellow or green on different occasions. The child always gained weight slowly. Feedings were always taken well, with no vomiting. Administration of viosterol in halibut liver oil was begun at 14 days, and this was changed to cod liver oil at 7 months. Orange juice was given at 20 days. At the age of 3 to 5 months the formula was grade B milk and 6 tablespoons of calcium caseinate to 1 quart (946 cc.) of milk and 6 ounces (177 cc.) of water. At 3 months the child began to receive jello, junket, ripe banana, scraped apple and fruit juices. At 4 months cereal was begun, and at 5 months strained vegetable and egg yolk were added. Fish and chicken were given for a few days before the child's admission. The appetite was excellent, and everything was consumed with relish. The infant sat alone at 6½ months and stood with support at 7 months, and the first tooth appeared at 8 months. The skin was dry but without eczema. After the age of 3 months there was constant discharge from the nose, with a cough which became progressively worse. The gain in weight was slow, none occurring between the ages of 5 and 8 months.

Physical Examination.—On admission the infant was small and active and did not appear ill (fig. 2). The weight was 6.3 Kg. There was a deep, almost brassy cough, which occurred in short paroxysms without whoop or vomiting. The abdomen was prominent and somewhat distended, the rectus muscles were somewhat separated, and there was a small umbilical hernia. There were dry rales at the bases of the lungs.

Laboratory Examination.—The hemoglobin content was 15.7 Gm. per hundred cubic centimeters; the red cell count was 5,000,000 and the white cell count 11,300, with 33 per cent polymorphonuclears, 62 per cent lymphocytes, 4 per cent monocytes and 1 per cent eosinophils. The urine was normal. The Kahn reaction was negative. The dextrose tolerance test gave the following values: control, 67 mg. per hundred cubic centimeters; 1 hour, 89 mg.; 2 hours, 86 mg. The urine contained no sugar. The values of the intravenous tolerance test with 5 Gm. of dextrose were as follows: fasting, 61 mg. per hundred cubic centimeters; 45 minutes, 92 mg.; 75 minutes, 55 mg.; 2 hours, 54 mg.; 3 hours, 53 mg. The calcium content of the serum was 9.4 mg. and the phosphorus content 4.7 mg. per hundred cubic centimeters. The carbon dioxide–combining power of the plasma was 37.6 volume per cent. Serum cholesterol values were as follows: total, 107 mg. per hundred cubic centimeters; free, 36.6 mg.; combined, 70.4 mg.; ratio of combined to free, 1.92. The total dry weight of a sample of the stool was 46.9 Gm.; the neutral fraction weighed 6.7 Gm.; the free fatty acid, 11.95 Gm., and the total ether-soluble material (lipoids), 18.65 Gm. (39.8 per cent); the ratio of free fatty acid in the total ether-soluble material was 64 per cent. The lipase content of the serum (tributyrinase) was normal. The amylase content of the blood (viscosimetric method) was approximately 0.56 units per cubic centimeter (normal, 0.08 to 0.25). The reaction to tuberculin was negative. The results of culture of material from various sources were as follows: stools, negative for typhoid and dysentery on repeated examination; nose, Str. haemolyticus, Staph. aureus and diphtheroids, later a pure culture of Pneumococcus type XIX; throat, Staph. aureus, Str. haemolyticus and a few pneumococci; left ear, Str. haemolyticus, later also Staph. aureus; right ear, Str. haemolyticus, later also Staph. albus and aureus. The serum did not agglutinate with Bacillus typhosus, B. paratyphosus A, B and C,

Bacilli dysenteriae Sonne, Shiga or Flexner, Bacillus abortus, or Bacillus melitensis. At the age of 8 months roentgen study of the chest and of the gastrointestinal tract gave negative findings. The forearms showed no rickets. There were transverse lines in both radiuses at 9 months. At this time the chest appeared normal, and the temporal bones showed a suggestion of exudate in the mastoid cells on the left.

Course.—Bilateral otitis media appeared and did not respond well to myringotomy. Both mastoids became infected. The stools were so foul as to require the isolation of the patient. She was given a high caloric diet for celiac disease, which did not alter the stools. The child was discharged after two and one half months in the hospital at the age of 10½ months; the weight was 6 Kg. She was readmitted at the age of 1 year because of fever and weakness. The weight was 5.3 Kg. Furuncles were present in the scalp. The abdominal distention had increased, and there was gluteal wasting. The appetite had decreased. At this time the hemoglobin content was 19.6 Gm. and the red cell count 4,750,000. Roentgen study of the chest showed bronchopneumonia, with heavy shadows in the lower part of the pulmonary field on the left, which were consistent with bronchiectasis or with multiple abscesses of the lung. The patient continued to lose weight and strength. Colonic irrigation produced great quantities of extremely foul grayish-green feces. The child was given iron, brewers' yeast, percomorph liver oil and, in the last three weeks, parenteral injections of liver extract. Nine days before death bronchopneumonia developed, and culture of material from the throat showed the type VI pneumococcus. The patient died three months after admission.

Autopsy.—The age at death was 14½ months, the weight 5.72 Kg. and the length 72 cm.

Gross Examination: The body was emaciated. The protuberant abdomen had a circumference of 48 cm. The anus was red, and the rectal mucosa protruded from its orifice and was inflamed. The arms and legs showed marked wasting. The peritoneal cavity contained 5 cc. of straw-colored fluid. There was a small amount of delicate fibrinous exudate over the serosal surfaces of the small intestine. The terminal portion of the duodenum joined the jejunum through an opening in the transverse mesocolon, which was 4 cm. in diameter. A finger passed through this opening came up between the two layers of mesocolon. The pleural and pericardial cavities appeared normal.

The ductus arteriosus admitted a fine probe.

The left lung bore a few fibrous tags on the posterior surface of the lower lobe. The anterior margin of the upper lobe, the lingula and the posterior surfaces of both lobes were purple, noncrepitant and depressed. The remainder of the lung was pink and aerated. The large bronchi were full of bright yellow, thick pus, which extended into the small bronchi. The walls of the small bronchi were somewhat thickened, and the lumens were slightly dilated. The hilar lymph nodes were enlarged and grayish red to deep red; they measured up to 1.5 cm. in length. The right lung bore subpleural punctate hemorrhages. The apex was purple, firm and sunken. The inferior portion of the lower lobe contained areas of consolidation, the largest measuring 2 cm. in diameter. The cut surface resembled that of the left lung. The larynx, trachea and main bronchi contained thick yellow mucoid pus. The mucosa was pink.

The spleen weighed 14 Gm. The cut surface was deep purplish red with indistinct malphighian corpuscles.

The liver weighed 380 Gm., was of normal consistency and was purplish red. The gallbladder and bile ducts were normal.

The pancreas was pinkish gray and of normal consistency. The main duct was patent throughout. There was some irregularity in the size of the lobules, and some of them were adherent to one another.

The intestines were thin walled. The upper portion of the small intestine contained fecal material, which was soft and bright yellow. The ileum and colon contained solid gray fecal material, which was so dry that the surfaces bore the imprint of the lymph follicles. The cecal mucosa appeared congested.

The heart, adrenals, kidneys, pelvic organs and ribs showed no abnormalities.

A thick green exudate was found in the ethmoid cells on the left and in the right maxillary antrum. The middle ears and mastoids appeared normal.

Microscopic Examination.—In one section of pulmonary tissue the bronchi were somewhat dilated and were filled with an exudate of polymorphonuclear leukocytes, phagocytes and débris. The bronchial epithelium was infiltrated with lymphocytes, plasma cells and a few polymorphonuclear leukocytes. Some of the alveoli contained a fresh purulent exudate. The remaining alveoli were emphysematous. The Gram stain showed that the bronchial and alveolar lumens were filled with clumps of gram-positive cocci resembling staphylococci. Another section was similar to the first except that the major portion of the alveoli contained an exudate.

In the trachea there was a slight inflammatory reaction of the mucosa. The epithelium was of normal height.

In the spleen the malpighian corpuscles were partly depleted of lymphocytes. In the centers of the corpuscles were large cells with deeply eosinophilic cytoplasm, some of which showed nuclear fragmentation. The pulp contained many red cells and some yellow pigment which stained for iron.

Most of the liver was normal. Beneath the capsule there was a zone where the fibrous tissue was increased around the portal areas. A few polymorphonuclear leukocytes were present, and there was some proliferation of the bile ducts. A number of multinucleated liver cells were seen near this. The stain for iron showed a small amount of hemosiderin in both liver and Kupffer cells. The trichrome stain showed an increase in connective tissue beneath the capsule and, to a lesser extent, around the portal areas throughout the section.

The acini of the pancreas varied greatly in size. Many resembled cysts and contained eosinophilic concretions, some of which were laminated. Some acini contained desquamated epithelial cells, lymphocytes and rare polymorphonuclear leukocytes. The epithelium was flattened. There was a marked increase in intralobular and interlobular connective tissue, in which occasional polymorphonuclear leukocytes and lymphocytes were noted. Some of the ducts were dilated and contained eosinophilic material. The islands were normal. Von Kossa's stain revealed that occasional concretions were calcified in the center (fig. 8).

The mucosa of the intestines was congested and contained lymphocytes, plasma cells and eosinophils. The lymph follicles were somewhat depleted of cells.

The other organs showed no abnormalities.

Bacteriologic Examination: Culture of material from the ethmoid sinus yielded Staph. aureus haemolyticus; of material from the peritoneum, no growth, and of the blood, no growth.

Anatomic Diagnosis: The diagnosis was celiac disease (clinical); cystic fibrosis of the pancreas; purulent laryngotracheobronchitis; lobular pneumonia due to Staphylococcus and Streptococcus; acute ethmoiditis on the left, due to Staph. aureus haemolyticus; acute maxillary sinusitis on the right; early biliary cirrhosis of the liver; congenital anomaly of the transverse mesocolon; patent ductus arteriosus, and hemosiderosis of the liver and of the spleen.

Case 44 (XX).—M. D., a girl, was the first child. She was first admitted to the hospital at the age of 23 months with the complaint of hunger and delayed development. She was born at term by breech delivery. The weight at birth was 6 pounds and 1½ ounces (2,764 Gm.). While in the hospital the infant lost 1 pound (454 Gm.) but otherwise appeared normal. Because of insufficient milk she was not nursed. The formulas were as follows: For the first three months, lactic acid, milk, Karo and water; for the next three months, malted milk; then, for a period not stated, soft-curd milk with chocolate; since the age of 13 months, evaporated milk and water. Administration of cereals was started at 4 months and stopped at 13 months, after which the child had very little starch. Vegetables were first given at 6 months; liver, lamb chops and bacon, at 7 to 9 months, and orange juice, at 2 months.

Cod liver oil and viosterol were given in winter but not in summer. At the time of admission the girl was being given all vegetables except potato. Her development had been delayed. The weight was as follows: at 6 months, 9 pounds (4,082 Gm.); at 12 months, 11 pounds (4,990 Gm.); at 23 months, 15 pounds and 6 ounces (6,974 Gm.) The first tooth appeared at 12 months; she sat at 12 months and walked with support at 10 months but had never walked alone. She was beginning to talk. She ate a great deal, yet never seemed satisfied and never gained well. At the age of 4 months, when first given cereal, she had large bowel movements. Before the age of 1 year she had persistent diarrhea, with about 8 stools a day; these were greenish and foul-smelling. During the twelve months before admission the stools were said to have numbered 1 or 2 a day; they were brown and soft but not frothy. Rectal prolapse occurred frequently. There was no nausea or vomiting. There had been no acute illnesses. The child was observed in the clinic for two weeks, being given a diet normal for an infant, and was then admitted for study.

Physical Examinaiton (fig. 2*B*).—The child appeared active but small. The head was large, with moderate frontal bosses. The buttocks were flat and the extremities thin and underdeveloped. The heart and lungs were normal. The edge of the liver was palpable, but the spleen and kidneys were not felt. The patient kept her head turned to the left.

Laboratory Examination.—The hemoglobin content was 13.6 Gm., the red cell count 4,600,000 and the white cell count 8,000, with 51 per cent polymorphonuclears, 46 per cent lymphocytes and 3 per cent eosinophils. The Kahn reaction was negative. The urine was normal. The stools numbered 1 to 3 daily; they were large, loose, gray and soapy, with foul odor. Repeated cultures were negative for typhoid and dysentery organisms. Analysis of stool showed that the moist weight was 57 Gm., with 67 per cent water; the ether-soluble material was 53.5 per cent of the dry weight and the material soluble in purified petroleum benzine 50.8 per cent, with free fatty acids in the sum of neutral and free fatty acid fractions, 69.1 per cent, and free fatty acids as soaps in the total free fatty acids, approximately 18.2 per cent. The calcium content of the blood serum was 10.2 mg. per hundred cubic centimeters; phosphorus, 4.3 mg.; albumin, 4.09 Gm., and globulin, 1.86 Gm. The dextrose tolerance test, after 1.75 Gm. of dextrose per kilogram of body weight had been given by mouth, gave these values: control, 52 mg. per hundred cubic centimeters; thirty minutes, 157 mg.; one hour, 204 mg.; two hours, 78 mg. There was no sugar in the urine. Roentgen study showed no evidence of rickets or syphilis. With a barium sulfate enema the colon and emptying time appeared normal. A series of roentgenograms showed that the gastrointestinal tract was normal except for some dilatation of the distal portion of the ileum.

Course.—The stools were typical of celiac disease. Proctoscopic examination showed nothing abnormal except prolapse of the rectal mucosa. The child was hungry but failed to gain with a diet standard for an infant. She was at first given a diet high in calories and soon after was transferred to a diet for celiac disorder, after which she did somewhat better. A tentative diagnosis of celiac disease was made.

For the year after her discharge at the age of 25 months she was followed in the clinic; she showed marked improvement with the regimen for celiac disease (fig. 2 *C*). The diet on her discharge consisted of 1¼ cups of banana powder (Merck), ½ cup of protein milk, 3½ cups of water, 3 eggs, 4 tablespoons of scraped beef, 2 tablespoons of vegetables, 6 tablespoons of cheese and 6 bananas. The girl gained weight and strength and ate ravenously. The stools remained fairly large, soft, yellow and foul. In other respects the child appeared normal, healthy and active.

At the age of 3 years the girl was readmitted to the hospital for operation for congenital torticollis. Her weight on admission was 27 pounds and 3 ounces (12.3 Kg.). On the second day after operation a temperature of 103.5 F. developed, and with it there appeared signs of pneumonia. Bilateral otitis media became evident during the following week. The patient died three weeks after the operation.

Autopsy.—This was done two hours post mortem. The age at death was 3 years and 2 months, the weight 9,750 Gm. and the length 92 cm.

Gross Examination: The skin was pale, and the body well nourished and fairly well developed. Over the right occiput there a small decubitus ulcer. A transverse scar 5 cm. in length extended from the suprasternal notch over the right clavicle. The chest was normal in contour. There was moderate abdominal distention. The subcutaneous fat was moderate in amount, and the muscles were well developed. The peritoneal cavity appeared normal. The liver extended 4.5 cm. below the xiphoid. The diaphragm was high and lay at the level of the third interspace on the right and the fourth rib on the left. The pleural cavities contained no free fluid, but the pleural surfaces bore a delicate fibrinous exudate.

The heart weighed 58 Gm. It appeared normal except for a patent foramen ovale with an opening 8 mm. in each diameter. The aorta was normal.

The right lung weighed 176 Gm. There were several small abscesses in the middle and in the lower lobe. The largest lay in the middle lobe, was multilocular and measured 1 cm. in diameter. The bronchial mucosa was thickened and congested. The tissue between the abscesses was mottled and uneven in consistency. The left lung weighed 158 Gm. It resembled the right. Small abscesses were scattered in both lobes.

The spleen weighed 26 Gm. It was bright red and soft, and the malpighian corpuscles were pale.

The liver weighed 738 Gm. It was large and pale yellow, and the margins were rounded. The lobulation was normal. The bile passages were normal.

The pancreas appeared to be about half the normal size, but it was not weighed. It was flabby and rather soft, but on section it was somewhat gritty. The lobules were irregular and appeared rounded. A prolonged search for the pancreatic duct revealed only a small duct which extended 8 mm. from the ampulla and was then lost in fibrous tissue.

The esophagus was moderately dilated in the lower half, and the epithelium was slightly thickened and congested. The stomach was small and normal. The

small and large intestines appeared normal except for moderate dilatation, especially of the colon. The colon contained a large amount of soft, putty-like, pale yellow fecal material throughout its length. There was no foul odor.

The other organs appeared normal.

Microscopic Examination: A section of the middle lobe of the right lung was taken through the multilocular abscess, which appeared as many small abscesses. Each abscess contained necrotic material surrounded by a wall of granulation tissue. In the remaining lung tissue the alveolar and bronchiolar walls were thickened and infiltrated with plasma cells and mononuclear phagocytes, and there was pus in the lumens of the bronchioles. The Gram stain revealed many pairs and short chains of gram-positive cocci in the abscesses. In another section the bronchi contained purulent material, and their walls were edematous and infiltrated with polymorphonuclear leukocytes and lymphocytes. There were irregular patches of recent bronchopneumonia.

There was congestion of the spleen. Small zones of red cells and a few polymorphonucler leukocytes were observed around the malpighian corpuscles. A little hemosiderin was present within phagocytes.

Nearly every liver cell was distended with a single large fat droplet. Otherwise the liver was normal.

A section from the body of the pancreas showed that the tissue (fig. 10) was composed of primary lobules about the size of a low power field, each of which was surrounded by and infiltrated with dense fibrous tissue. Within each lobule there were irregular clumps of tubules or cysts. Most of the tubules were composed of columnar epithelial cells without granules around a larger or smaller lumen, in which was a mass of homogeneous eosinophilic material resembling hyaline casts or corpora amylacea. The larger cysts were lined by flattened or cuboidal epithelium and contained granular protein precipitate or a large mass of hyaline material. These cysts and tubules were separated from one another by dense fibrous tissue in which there were occasional lymphocytes. None of the acini appeared capable of normal function. The islands appeared normal in number. Many were surrounded by a widened peripheral sinus, but they were not otherwise abnormal. There was no evidence of acute inflammation. A section from the head of the pancreas was similar to the section from the body. Many of the lobules were replaced by fat. The islets were small and less numerous than in the first section.

The cortical lipoid of the adrenal was scanty. There were hemorrhages in the capsule and in the fat near the gland.

A section of kidney was normal.

In the esophagus there was extensive ulceration of the epithelium, leaving a surface of submucosa densely infiltrated with lymphocytes and large phagocytes. Beneath the surface the submucosa was greatly thickened by edematous and recently formed fibrous tissue in which many fibroblasts and congested vessels were noted.

The stomach was normal except for several small collections of lymphocytes in the deeper layers of the mucosa.

The mucosa of the jejunum was infiltrated with lymphocytes, and large phagocytes and fibroblasts were present. The infiltration was most marked in the villi, which were thereby much thickened. The infiltration was about equal in degree throughout the mucosa (fig. 4).

The colon was similar to the jejunum except that the infiltration of the mucosa was less marked.

The rib was normal. There was no evidence of old or recent rickets.

Bacteriologic Report: Cultures of the lung showed Str. haemolyticus and Staph. aureus haemolyticus. Cultures of the blood, material from the pleural cavity and the spinal fluid were negative.

Anatomic Diagnosis: The diagnosis was celiac disease (clinical); cystic fibrosis of the pancreas; congenital atresia of the pancreatic duct (?); chronic enterocolitis; hypertrophy of the colon; torticollis (clinical); operative division of both heads of the right sternocleidomastoid muscle; otitis media (clinical); abscess of the middle lobe of the right lung; purulent bronchitis; lobular pneumonia (Str. haemolyticus and Staph. aureus haemolyticus); acute fibrinous pleurisy; acute splenic tumor; fatty liver; ulcers of the esophagus and congenital malformation of the heart (patent foramen ovale).

Summary.—This patient was considered to have fairly characteristic celiac disease, which began at the age of 4 months, with underdevelopment, malnutrition and typical stools. Chemical examination of the stools showed an approximately normal percentage of digested fat, a finding usually thought to eliminate the possibility of pancreatic steatorrhea. The impression that the child had celiac disease was strengthened by her extraordinary improvement on a diet for this condition (fig. 2 *B* and *C*). At autopsy no normal acini were found in the pancreas (fig. 10). The pancreas appeared to consist entirely of fibrous tissue, cysts and round islands of Langerhans. The pancreatic duct could not be followed more than 8 mm. from the ampulla of Vater. Death resulted from postoperative bronchopneumonia.

Case 28 (XXII).—This was contributed by Dr. Paul Klemperer of Mount Sinai Hospital. J. D., a sister of M. D. (case 23 [XV]), was a first child and was born approximately eighteen months before her brother. She was under the private care of a series of physicians, and consequently the details of her clinical course were difficult to ascertain. Her mother stated that she presented a feeding problem and had loose stools from birth. Her diet was changed many times. Because of intolerance of fats the fat of the diet was limited, and it is probable that she did not receive adequate amounts of the fat-soluble vitamins A and D. She did not have symptoms of ocular disease. Her development was subnormal. At 4 months she began to have a discharge from the nose and at 7 months a chest cold and cough developed. The infant died at the age of 8 months.

Autopsy was performed at the Mount Sinai Hospital. The infant was poorly developed and nourished. The following note occurs on the protocol: "An unusual picture was presented by the pancreas. There was diffuse pancreatitis and marked dilatation of the ducts. The picture was one of chronic pancreatitis of unexplained etiology." The accessory pancreas in the jejunum presented a similar picture.

The anatomic diagnosis was acute and chronic mucopurulent tracheitis; bronchitis and bronchiolitis with bronchial dilatation; chronic peribronchitis; suppurative pneumonia (middle and lower lobes, right lung); chronic pneumonitis (lower lobe, right lung); bronchopneumonia (upper lobe, right lung; lower lobe, left lung); fibrinous pleuritis (middle and lower lobes, right lung); parenchymatous degeneration of the liver; acute congestion of the viscera, and aberrant pancreas in the jejunum.

Dr. Klemperer has permitted me to study the sections of the pancreas and of the lung. The pancreas was closely similar in appearance to that of M. D., the brother (case 23 [XV]), and the lung was also similar to the brother's except that there was more marked hyperplasia of the bronchial epithelium in the present case.

Note.—Reports of additional cases are included in the author's reprints.

DISCUSSION

Dr. Frederic H. Bartlett, New York: I should like to cite the instance of an infant who was admitted to the hospital at the age of 6 weeks and died at 3 months. Her weight at birth was 7 pounds and 5 ounces (3,317 Gm.), and she was well up to the eighth day of life. She was weaned because of the mother's infected breast. Many changes were made in her food: She was given breast milk, three trials at similac, breast milk again and protein milk; before she died she was taking protein milk and breast milk. Her appetite, as a rule, was fairly good during all this period. That is curious because her stools were at times loose and at times good. She did not gain weight, and her failure to gain was so persistent that my associates and I were puzzled. At the age of 7 weeks the child had pulmonary symptoms, which went on until she died, at the age of 3 months. This pulmonary condition was clinically diagnosed as pneumonia. The pathologic changes in this child were bronchopneumonia, cystic fibrosis of the pancreas, patent ductus arteriosus and patent foramen ovale.

The mother had another child, who died at the age of 8 weeks; she made this extraordinary statement: "Whatever my first baby had, this baby has too." It is interesting that this condition has been found in members of the same family. In such cases there is this fairly clear clinical entity: The infant is born looking well, has the proper weight and is fed with care; however, the child does not gain weight in spite of proper food; the bowels may or may not be loose; pulmonary infection supervenes. There is no vomiting, but the infant simply refuses to survive. As physicians look back over their records, they are often puzzled as to why a child who looked all right and who seemed to be in good condition died within the first four or five months of life with nothing to account for it.

In summary: Cystic fibrosis of the pancreas is a nucleus about which is being crystalized a symptomatology. The condition should be considered a new clinical entity, and I feel that Dr. Andersen has contributed a great piece of work in that connection.

Dr. Benjamin Kramer, Brooklyn: I wish to record 2 cases which I believe belong to this group; the patients were members of the same family. The little girl died at the age of 7½ months and the boy at the age of 2½ years. The clinical symptomatology will be presented in a detailed report by my associates. I want merely to present a few sections illustrating the pathology of this disease.

The first is a section from a normal pancreas, showing the meager amount of connective tissue between the acinar tissue and some of the islands of Langerhans. The second section, from the pancreas of the 7½ month old patient, shows the extensive fibrosis of the gland, with a few isolated acini and an apparent increase in the amount of island tissue. There are no cysts of the acinar tissue, but there is dilatation of the ducts. Other sections from the same pancreas show dilatations of the acini, which were filled with pink-staining material. The sections from the lung show a purulent exudate in the bronchioles, with infiltration of the bronchial walls and involvement of the peribronchial tissue. Emphysema of the lung is also present. A section of the liver shows almost complete filling of liver cells with fat. The nuclei are compressed to the cell periphery. Permission for an autopsy on the older child was not obtained, but the clinical course was so similar to that of his sister that there is little doubt that both suffered from the same disease.

Another interesting point in this connection was the early appearance of pulmonary symptoms. Both children had respiratory symptoms, including wheez-

ing and cough, during the first few months of life. These recurred from time to time. The terminal pulmonary condition began with asthmatic bronchitis, which developed into purulent bronchitis, bronchiolitis and finally bronchopneumonia. No histologic evidence of vitamin A deficiency was observed.

My associates and I favor the view that this is a distinct clinical entity which may be both congenital and familial. Although the symptoms may superficially resemble those of celiac disease and the patient may temporarily respond favorably to a regimen for the latter condition, the early onset of symptoms, which often begin at birth, the high mortality of this disease, the marked tendency of these patients to contract fatal diffuse bronchopneumonia and the peculiar pancreatic lesion separate this condition definitely from true celiac disease, which has been described by Gee and others.

DR. WILBURT C. DAVISON, Durham, N. C.: Could celiac disease in children, which apparently is the same syndrome as sprue in adults, be due to temporary damage or impairment of the pancreas? The activity of the duodenal enzymes and the ability to digest and absorb carbohydrates are reduced in celiac disease.

DR. LOUIS K. DIAMOND, Boston: During the past few years Dr. Blackfan, Dr. Wolbach, Dr. Farber and Dr. May have been engaged in correlating the clinical and pathologic manifestations of infants and children who presented these important changes in the pancreas.

In addition to 28 examples of this condition in its most severe forms, noted prior to 1935, they have observed minor degrees of changes of this nature in well over 100 patients of ages ranging from birth through early childhood.

The histologic picture in the 28 severely affected children has been strikingly uniform and apparently similar to that described by Dr. Andersen. The sequence of events, as outlined by Blackfan and Wolbach in 1933, appears to be as follows: An abnormal secretion is produced. This becomes inspissated, which leads to distention of the ducts and atrophy of the acini. Subsequently fibrosis occurs. The cause of this pancreatic lesion has not been determined. There are insufficient data concerning the role which the lesion plays in producing the clinical entity known as celiac disease.

It is to be expected that any interference with the absorption of fat might interfere with the absorption of vitamin A, but direct chemical studies of the blood and of the liver of 1 patient who at necropsy had these severe lesions in the pancreas showed that this child was able to absorb vitamin A if an adequate quantity was present in the food. Consequently, although absorption of vitamin A might be diminished, it would not be entirely absent if the patient's diet were adequate and especially if infection were not a complicating factor.

In this series of 28 cases, most of the patients were suffering from severe nutritional disturbance, complicated in many instances by chronic bronchopneumonia. Pathologically, 2 patients also showed the changes of vitamin A deficiency, 3 had meconium ileus, and 1 had hepatic cirrhosis. The symptoms of disease appeared early in life: at birth in 2 infants, before the age of 2 months in 2 others and before 9 months in the remaining 22 patients.

That this lesion is the underlying cause of celiac disease seems questionable. In only 3 of the 28 children with the severe fibrosis in the pancreas did the symptoms suggest a possible celiac state, and in only 1 instance were there confirmatory laboratory findings such as a flat dextrose tolerance curve, the clumping of the barium sulfate in the small intestines seen in roentgen study of the gastrointestinal tract, osteoporosis observed by roentgen examination and deficiency of minerals.

Also against the suggestion that the celiac syndrome is always the result of this particular pancreatic lesion, or even that it usually may play a part in its production, is the authoritative opinion of Parsons, who recently reviewed the necropsy observations in 12 cases of celiac disease and was unable to detect any pathologic changes in the pancreas.

Dr. L. Emmett Holt Jr., Baltimore: I hope Dr. Andersen will tell us how she feels about the relation of vitamin A deficiency to this picture. Some of the patients described in the literature were classified as having vitamin A deficiency; so I suppose there was definite evidence of this in some cases and not in others.

Dr. Frederic W. Schlutz, Chicago: I should like to know whether in the cases reported in the literature the pulmonary symptoms preceded the pancreatic symptoms. About a year ago my associates and I had under our care a boy 6 years of age who had had pulmonary symptoms and bronchiectasis since infancy and what appeared to be symptoms of celiac disease since the age of 4 years. On admission to the hospital the boy seemed to have pronounced evidence of the latter condition along with advanced bronchiectasis. Further study of the case, however, convinced us that he did not have celiac disease but was suffering from chronic fibrotic disease of the pancreas. The boy died of terminal pneumonia. At autopsy complete chronic cystic fibrosis of the pancreas and extensive bronchiectasis with a superimposed recent pneumonic process were noted. There was no gross or microscopic evidence of vitamin A deficiency. The possible association of vitamin A deficiency with this condition is interesting and should be carefully checked.

Dr. Dorothy H. Andersen, New York: I have had no experience with sprue. It seems to me that the mechanism in pancreatic disease is complicated; I think the condition must be related in some way to sprue, but as yet this relation is unknown.

In regard to the cases presented, I should have said that in one third of the cases of the entire series there was fatty liver.

My statement about celiac disease did not imply that the pancreatic lesion is the cause of celiac disease in all cases but indicated that all of our patients with cystic fibrosis of the pancreas who survived the first year of life were clinically indistinguishable from those with the classic picture of celiac disease and that therefore it seems reasonable to refer to a celiac syndrome which may be produced by this disease entity or by one or more others.

In my search through the literature for cases of celiac disease in which there was autopsy with examination of the pancreas, I have found only 11. There were many more cases of celiac disease in which autopsy was done without examination of the pancreas. Clinical celiac disease is not as rare as the scarcity of reports would indicate, but I feel that in many instances other conditions observed post mortem, such as bacillary dysentery or the pancreatic lesion, may have altered the diagnosis. It would seem that the patients with celiac disease who survive to adult life have not had a severe pancreatic lesion. At present I do not know how to distinguish cystic fibrosis of the pancreas from early celiac disease except by examination of the duodenal juice for enzymes or by postmortem study of the pancreas.

The question as to whether vitamin A deficiency and the pulmonary lesion precede the pancreatic symptoms is an involved one. There is good evidence that the pancreatic lesion is present at birth or early in life, and in only 2 of the 44 patients who survived the neonatal period was there any evidence of infection during that period. In some cases the digestive symptoms were not noticed until after the

neonatal period. If the lesion is present at birth—and it is known that it can be present because it has been observed in 5 patients who died before the age of 1 week—one cannot imagine that it is due to dietary vitamin A deficiency. There remains the possibility that the pancreatic lesion results from vitamin A deficiency during the time of gestation; congenital vitamin A deficiency is a question about which little is known.

I do not know the cause of this disease. There is a good deal of evidence to show that at least in the majority of cases the pancreatic lesion comes first. In only 12 of the 44 cases was there histologic proof of vitamin A deficiency; in 2 there was xerophthalmia and in all 12 cases there were metaplastic changes in the epithelium. All the 44 patients had pulmonary lesions which were primary in the bronchi, and many had bronchiectasis. Of 12 previously reported cases of vitamin A deficiency in infants on whom postmortem examination was done, the pancreas was described in 7, and in all 7 cystic fibrosis of the pancreas was noted. This is too high a percentage to be accidental. The evidence at hand suggests that the pancreatic lesion prevents the normal digestion and absorption of fats, the poor absorption of fats results in poor absorption of the fat-soluble vitamin A and the epithelial metaplasia, bronchiectasis and bronchopneumonia are consequences of vitamin A deficiency. I do not understand why metaplasia of the epithelium is present in some cases and not in others.

Abstracts from Current Literature

Biochemistry; Bacteriology, and Pathology

A New Method for the Evaluation of Germicidal Substances. A. J. Salle, W. A. McOmie and I. L. Shechmeister, J. Bact. **34**:267 (Sept.) 1937.

The authors feel that the determination of the phenol coefficient is not an accurate basis for evaluating disinfectants to be employed under all conditions. The method is practical for rating disinfectants to be employed for the sterilization of nonliving material. On the other hand, the method fails to take into account the toxicity for living tissues of germicides which are to be used internally or on mucous surfaces. A more valuable expression is one based on a combination of the titer of the killing power of the disinfectant for bacteria with that of its toxic action toward living embryonic tissue. This gives a figure which is known as the toxicity index. The toxicity index is defined as the ratio of the highest dilution of disinfectant required to prevent the growth of embryonic chick heart tissue during forty-eight hours to the dilution required to kill a given test organism in ten minutes. The toxicity indexes are not always proportional to the phenol coefficients. Iodine trichloride and metaphen have the same phenol coefficient, yet metaphen is about thirty-two times as toxic to embryonic chick heart tissue as the iodine compound. As a germicide, merthiolate is over a hundred times more potent than mercurochrome but only about one-eighth as toxic to tissue.

An important observation is that the older and simpler germicides rate considerably higher than the newer and more complex compounds. Iodine is one of the oldest germicides known. It is usually employed as a tincture of iodine, an alcoholic solution, which is quite irritating, owing to the presence of the alcohol. Because of this irritating property, the alcoholic solution is gradually losing favor. In aqueous solution the iodine is nonirritating and relatively nontoxic to tissue. It is the most ideal of any of the compounds studied when tested by the tissue culture technic.

Stoesser, Minneapolis.

The Fusobacterium Genus: I. Biochemical and Serological Classification. E. H. Spaulding and L. F. Rettger, J. Bact. **34**:535 (Nov.) 1937.

Fusiform bacilli are normally present in human mouths and throats and on the external genitalia, also in the oral cavities of animals of various species. They have been observed in man in various pathologic conditions. In spite of their frequent occurrence in nature, there has been little progress in the classification of these organisms since Leiner (1907) first observed that there was more than one cultural type. This situation may be ascribed largely to the difficulty of obtaining satisfactory growth on solid medium. Spaulding and Rettger have tried to bring present knowledge of fusiform bacilli up to date. Their report deals with a morphologic, cultural, biochemical and serologic study of 80 strains originating from a variety of sources. All of the cultures were gram negative, nonmotile, nonsporulating and, when isolated, strictly anaerobic. The 80 strains of Fusobacterium could be divided into two main groups by their biochemical and serologic behavior. Group 2 is distinguished from group 1 by (*a*) its ability to produce approximately twice as much acid from carbohydrates as the latter group, (*b*) its property of fermenting maltose and trehalose and (*c*) its inability to form indole, to produce hydrogen sulfide and to reduce nitrates. Each of the two groups is made up of two important fermentative subgroups or types. A method for preparing satisfactory antigens for the agglutination test is described. The precipitin technic, however, failed to yield reliable results.

Stoesser, Minneapolis.

THE FUSOBACTERIUM GENUS: II. SOME OBSERVATIONS ON GROWTH REQUIREMENTS AND VARIATION. E. H. SPAULDING and L. F. RETTGER, J. Bact. **34**:549 (Nov.) 1937.

In a previous communication Spaulding and Rettger separated Fusobacterium into two main groups on the basis of biochemical and serologic properties. The present report deals with the morphologic and cultural characteristics of these groups, with emphasis on nutritional requirements and variation. The morphologic characteristics of the fusobacteria are variable but conform in general to the proposed groups 1 and 2. The character of the growth in broth constitutes a valuable criterion for differentiating the two groups. The growth requirements are of a widely divergent nature. Vigorous development of both groups is supported by a potato extract medium containing dextrose and cysteine. The nutritive and anaerobic requirements are influenced greatly by artificial cultivation. A granular type of growth in broth and an opaque colony on agar are manifestations of bacterial variation. Spiral forms are of rare occurrence in laboratory mediums. Some of the fusiform bacilli may be pathogenic for laboratory animals, but no evidence of toxin production could be obtained.

STOESSER, Minneapolis.

AN ATTEMPT TO PURIFY BACTERIOPHAGE BY THE PROCEDURE OF VINSON. J. BRONFENBRENNER and S. E. SULKIN, J. Infect. Dis. **61**:259 (Nov.-Dec.) 1937.

In attempting to purify bacteriophage by the procedures developed by Vinson for the purification of the virus of tobacco mosaic, it was found that safranin removed the active agent from the lytic filtrates. However, despite the fact that the bulk of the bacteriophage was adsorbed on the safranin, the precipitate exhibited only mere traces of activity, and in the case of megatherium phage, none. This loss of activity was not due to the photodynamic effect of safranin. Neither elution with an especially fine prepared fullers' earth nor adjustment of the hydrogen ion concentration of the solution over a wide range was effective in setting free the active agent. Although the total nitrogen content of the supernatant fluid was approximately 14 per cent lower than that of the original lytic filtrate, the fact that its activity was reduced at best to one millionth of the original makes this method unsuitable for the purification of bacteriophage.

TOOMEY, Cleveland.

ACTION OF NORMAL AND DIABETIC SERA ON ANIMAL LIVER GLYCOGEN IN VIVO AND IN VITRO. O. L. V. DE WESSELOW and W. J. GRIFFITHS, Lancet **2**:670 (Sept. 18) 1937.

De Wesselow and Griffiths found that when serum obtained from fasting human beings was injected into rats there followed a reduction in their hepatic glycogen, the percental reduction being the same whether normal or diabetic serum was used.

Human serum accelerated glycogenolysis in the rabbit's liver in vitro, but no such effect was observed in the rat's liver.

To the authors it seemed unlikely that the effect of the injection of the serum on the glycogen in the rat's liver was due to amylolytic ferments in the serum.

LANGMANN, New York.

BACTERIOSTATIC ACTION OF P-AMINOBENZENESULPHONAMIDE UPON HEMOLYTIC STREPTOCOCCI. H. FINKLESTONE-SAYLISS, C. G. PAINE and L. B. PATRICK, Lancet **2**:792 (Oct. 2) 1937.

The authors found that the bacteriostatic action of sulfanilamide on hemolytic streptococci is preceded by a phase of stimulation of growth, more conspicuous in young cultures.

Sulfanilamide was found to be more soluble in the fatty envelop which can be separated from hemolytic streptococci than in aqueous solution. It stimulates the phagocytic activity of the reticuloendothelial cells of rabbits. It also stimulates the production of polymorphonuclear leukocytes in the bone marrow or rabbits.

LANGMANN, New York.

Metabolism; Infant Feeding; Milk and Other Foods

NUTRITIONAL EDEMA IN THE DOG: V. DEVELOPMENT OF DEFICITS IN ERYTHROCYTES AND HEMOGLOBIN ON A DIET DEFICIENT IN PROTEIN. A. A. WEECH, M. WOLLSTEIN and E. GOETTSCH, J. Clin. Investigation **16**:719 (Sept.) 1937.

In dogs maintained on a diet deficient in protein for from eighty to ninety days, the following changes were found: a progressive loss of body weight; a progressive decrease in blood volume; an initial rise and later a progressive fall in the relative cell volume, red cell count and hemoglobin concentration of the whole blood; a progressive decrease in the volume of the circulating red cells, and an initial rapid fall in the volume of the circulating plasma for about thirty days, after which time the volume remained constant. At the end of the experiments, in terms of percentages of original values, the serum albumin had suffered the greatest relative depletion, the hemoglobin was somewhat less involved, and the serum globulin was only slightly affected. In absolute amounts of protein removed from the circulation, the loss was six times as great for hemoglobin as for serum albumin, and seven times as great for serum albumin as for serum globulin. When total losses of protein from the body were compared, it appeared that about one fifth of the losses were from the circulation and four fifths from tissues outside the blood stream. A group of clinical patients acquiring or recovering from deficits in serum albumin was cited in whom the results of serial determinations of hemoglobin could be interpreted in the light of the associated changes in plasma volume.

GUEST, Cincinnati.

THE COMPARATIVE NUTRITIVE VALUES OF GLUCOSE, FRUCTOSE, SUCROSE AND LACTOSE WHEN INCORPORATED IN A COMPLETE DIET. H. H. MITCHELL, T. S. HAMILTON and J. R. BEADLES, J. Nutrition **14**:435 (Nov.) 1937.

The authors were aware that previous reports from various other workers showed that the various sugars, when ingested separately, may reveal a distinct difference in rate of absorption and of utilization and in physiologic effects.

In the present experiment it was found that in rats the sugars studied revealed little difference in their physiologic effects when they were fed as components of a complete diet. That, in fact, "administered in a complete diet, the nutritive values of the sugars appear to be very much the same except for differential effects on the digestibility of the organic nutrients of the rations."

MUNNS, Winnetka, Ill.

SUBSTITUTION OF OLIVE OIL FOR BUTTER FAT IN INFANT FEEDING. M. L. BLATT and E. H. HARRIS, J. Pediat. **11**:455 (Oct.) 1937.

Holt and his co-workers demonstrated that the fats with higher iodine value are more completely absorbed than the more saturated fats. Blatt and Harris studied the clinical effect of substituting olive oil having an iodine number of approximately 90 for butter fat having an iodine number of about 35, in the diet of a series of premature and newborn infants. The diet took the form of a powder composed of the following foods in the percentages given: skim milk, 40.6; virgin olive oil, 17.5; dextrimaltose, 31.7; calcium caseinate, 10.1; mineral ash, 3, and halibut liver oil, 0.1. The infants took the feedings well and tolerated them well. In growth and development they compared favorably with infants fed human or

evaporated milk. A study of the stool lipids confirmed the work of Holt and his co-workers in which they demonstrated that unsaturated long chain fatty acids, such as those found in olive oil, are better absorbed than the more saturated acids of cow's milk. The authors recommend the formula given as a complementary or substitute feeding for both normal and premature babies.

RAUH, Cincinnati.

HYPOGLYCEMIC ACTION OF ALLOXAN. H. R. JACOBS, Proc. Soc. Exper. Biol. & Med. **37**:406 (Nov.) 1937.

Alloxan ($C_4H_2N_2O_4 + H_2O$) is perhaps the only substance other than insulin so far found which causes hypoglycemia. If upward of 20 mg. of alloxan monohydrate per kilogram of body weight is injected intravenously into rabbits, the level of the blood sugar will rapidly drop and convulsions will occur. The convulsions are immediately relieved by dextrose administered intravenously.

HANSEN, Minneapolis.

THE INTERMEDIATE METABOLISM OF CARBOHYDRATES. H. A. KREBS, Lancet **2**:736 (Sept. 25) 1937.

Szent Györgyi in 1935 and 1936 reported experiments that suggested that succinic acid and its derivatives (fumaric acid, malic acid and oxaloacetic acid) catalytically promote oxidations in muscle tissue. Stare and Baumann in 1936 presented conclusive proof of this catalytic effect. Krebs and Johnson in 1937 found that citric acid also acts as a catalyst. In minute quantities added to muscle it accelerates the oxidation of carbohydrates. Martins and Knoop discovered that alphaketoglutaric acid is a product of the oxidation of citric acid.

Two cycles have to be considered:

1. Citric Acid Cycle

→ oxaloacetic acid + carbohydrate derivative (pyruvic acid?)

I. ↓ citric acid

II. ↓ ketoglutaric acid

III. ↓ succinic acid

IV. ↓ fumaric acid

V.

2. Szent Györgyi's Cycle

(*a*) oxaloacetic acid + "hydrogen of organic molecules" → succinic acid

(*b*) succinic acid + O_2 → oxaloacetic acid + H_2O

LANGMANN, New York.

KETONEMIA IN INFANCY. C. H. GRAY, Lancet **2**:1017 (Oct. 30) 1937.

In determining ketonemia in infants Gray used the colorimetric method of Behre and Benedict. Ketonemia develops much less readily in infants under 3 months of age than in those above that age. Autopsy in 108 cases of fatal vomiting with and without diarrhea indicated that in infants over 3 months of age with this disease the liver tends to become fatty, while in those under this age it is far less liable to this change. The explanation of the curious difference with respect to age must remain at present a subject for conjecture.

The ketone values for the blood of healthy infants were found to vary from 1.4 to 2 mg. per hundred cubic centimeters of whole blood. Vomiting infants under 3 months of age showed slightly higher values (from 1.6 to 4.5 mg.) whereas those over 3 months showed considerably higher values (from 2 to 19 mg., with 70 per cent over 4.5 mg.).

LANGMANN, New York.

EFFECT OF SUGAR AND OF INSULIN ON THE BLOOD SUGAR AND BLOOD PHOSPHATE CURVES OF THE CHILD. A. PERIN, Riv. di clin. pediat. **35**:980 (Nov.) 1937.

Perin studied the effect of the ingestion of 30 Gm. of sugar with and without the injection of 3 units of insulin on the blood sugar and blood phosphate curves of 17 fasting children. With or without insulin the blood phosphate falls, returning to normal in about two and one-half hours.

When 8 rabbits were given insulin, the blood phosphate fell during the first thirty minutes but returned to normal within one hour in 5 cases; in 2 rabbits the fall in blood phosphate was more prolonged.

The conclusion is drawn that insulin—both that given by injection and that produced in the baby on stimulation by an intake of sugar—affects the ionic equilibrium of the blood by causing a marked fall in the inorganic phosphorus.

HIGGINS, Boston.

THE FEEDING OF SICK INFANTS WITH WHOLE DRY ACIDIFIED MILK. G. PAISSEAU and E. BOEGNER, Bull. Soc. de pédiat. de Paris **35**:73 (Jan.) 1937.

The feeding of whole dry acidified milk gave good results, especially for young infants deprived of breast milk. A high caloric concentrated mixture of smaller volume than is usually possible with ordinary milk mixtures can be used. It was well tolerated by poorly nourished infants with digestive disturbance and by a number of infants during convalescence after diarrhea.

BENJAMIN, Montreal, Canada.

BREAST, BOTTLE AND MIXED FEEDINGS. G. ACCORDINI, Lattante **8**:168 (April) 1937.

Statistics on infants cared for in a maternity home are compared with statistics on infants observed in a clinic. Both morbidity and mortality rates were higher in the institution. Rickets was, however, slightly more common among the patients of the clinic. In the institution 56 per cent were wholly breast fed, 33 per cent were partly breast fed and 9 per cent were artificially fed; in the clinic 49 per cent were breast fed, 25 per cent were partly breast fed and 26 per cent were artificially fed.

HIGGINS, Boston.

STUDY ON OXALIC ACID OF MILK. G. FROLA, Riv. di clin. pediat. **35**:919 (Oct.) 1937.

Oxalic acid is present in both mother's milk and cow's milk. In mother's milk the quantity is usually between 10 and 15 mg. per hundred cubic centimeters; cow's milk contains about 20 per cent more than mother's milk. The diet of the mother, the period of nursing and the duration of nursing do not seem to make any appreciable difference in the amount of oxalic acid in the milk. Oxalic acid is present also in the colostrum. It should be regarded as a physiologic component of milk.

HIGGINS, Boston.

LACTARIUMS FOR HUMAN MILK. M. B. FILHO, Ann. de pediat., San Paulo **1**:91 (Nov.) 1937.

This is a very interesting article on the development of stations for the collection of breast milk. These are much more elaborate than any in this country.

A photograph shows 17 mothers sitting around a multiple pump having their breasts pumped simultaneously. SANFORD, Chicago.

BUTTERMILK IN THE TREATMENT OF INFANTILE TOXICOSIS. ARTURIO JOHNSON ORTIZ, Rev. Soc. de pediat. de Rosario **2**:143 (Sept.) 1937.

Four patients with extreme diarrhea and dystrophy were successfully treated with a buttermilk diet. SANDFORD, Chicago.

THE CALCIUM BALANCE IN NORMAL AND NEUROPATHIC CHILDREN. F. ROSSELLO, Rev. Soc. de pediat. de Rosario **2**:161 (Sept.) 1937.

In 15 normal children the maximal calcium content of the blood was 11.27, the minimal 10.05 and the average 10.38 mg. per hundred cubic centimeters. In 17 neuropathic children of the same age the maximal calcium content was 11.02, the minimal 10.06 and the average 10.23 mg. The median ratio was therefore 10.38 : 10.23. SANFORD, Chicago.

EXPERIMENTAL STUDIES OF CRANIOTABES: INORGANIC URINARY CONTENT OF RABBITS FED ON LACTOSE AND SUCROSE. T. YOSHINARE, Acta pædiat. japon. **43**:673 (May) 1937.

The urinary output of rabbits fed on lactose is decreased and its content of inorganic phosphorus, potassium and magnesium diminished. The urinary calcium, however, is decidedly increased. The decrease in urinary chlorides is not due to the effect of lactose. When the animals are fed sucrose somewhat similar changes take place, though not quite so extensively as with lactose. KATO, Chicago.

EFFECT OF DEXTROSE ON THE FULMINATING SYMPTOMS OF INTOXICATION. Y. MIYOSHI, Acta pædiat. japon. **43**:1221 (Aug.) 1937.

Following the suggestion made by Mita that the fulminating symptoms frequently seen in patients with acute colitis are due not to bacterial or chemical toxins but to abnormal stimulation of the blood vessels and of the autonomic nervous system, Miyoshi sought to treat these patients with some substance which would effect dilatation of the blood vessels. Basing his observations on experiments with animals he employed for this purpose a hypertonic solution of dextrose. A 25 per cent solution of dextrose, when injected by the usual method, produces a lowering of blood pressure both in normal animals and those narcotized with ethyl carbamate (urethane), and this effect is observed in equal degree after vagotomy and atropinization. The observation proves that the lowering of blood pressure is independent of stimulation of parasympathetic centers or of widening of the blood vessels. Hypertonic dextrose solution also increased the cardiac amplitude in the isolated rabbit heart, even after the blood pressure had fallen. The average blood flow in the coronary arteries was but slightly increased. The increase in the volume of the intestines and of the kidneys after the injection of hypertonic dextrose solution is probably due to dilatation of the blood vessels. The application of this therapeutic procedure in the management of acute colitis resulted in maintaining a high average percentage of recovery (89.6 per cent in a total of 75 cases). KATO, Chicago.

INDIVIDUAL VARIATIONS IN THE RELATION BETWEEN UREA CLEARANCE AND CREATININE CLEARANCE. J. BING and T. BJERING, Acta med. Scandinav. **93**:318, 1937.

Earlier investigations have shown that the relation of the urea clearance to the creatine clearance (a quotient of about 0.5) is fairly constant in both normal persons and persons with nephritis. The present work shows that in some persons with nephrosis the quotient may be much higher or lower (from 0.25 to

0.75). The abnormal ratio may be constantly high or constantly low, suggesting individual variations, but in one patient the variations during a three year period of observation were much wider than could be explained by such factors as diet and diuresis.

KAJDI, Baltimore.

MILK CLOTTING-MECHANISM AND MODIFICATION. I. N. KUGELMASS, Acta pædiat. **20**:29, 1937.

Kugelmass describes some physicochemical experiments designed to elucidate the phenomena involved in the coagulation of milk and elaborates an explanatory hypothesis based on these experiments.

McCUNE, New York.

Vitamins; Avitaminoses

MACROCYTIC ANEMIA IN PREGNANT WOMEN WITH VITAMIN B DEFICIENCY. KATHERINE O'SHEA ELSOM and ALBERT B. SAMPLE, J. Clin. Investigation **16**:463 (May) 1937.

The following hematologic changes which developed late in pregnancy in 8 women were believed to be due to dietary deficiency in vitamin B: a decrease in the number of red blood cells; an increase in the size and hemoglobin content of the erythrocytes; reticulocytosis, and the appearance in the blood smear of polychromatic cells, poikilocytes and immature white blood cells. Clinical disturbances were: glossitis and ulceration of the tongue, impairment or loss of the vibratory sense, tachycardia, edema and gastrointestinal symptoms, fatigue and paresthesia. The hematologic and clinical changes responded to brewers' yeast administered orally or to liver extract given intramuscularly.

GUEST, Cincinnati.

NITROGEN, SULFUR, SODIUM, POTASSIUM AND CHLORIDE METABOLISM IN VITAMIN B_1 DEFICIENT RATS. M. SANDBERG, DAVID PERLA and OLIVE HOLLY, Proc. Soc. Exper. Biol. & Med. **37**:350 (Nov.) 1937.

In rats deficient in vitamin B_1 there was evidence of disturbed protein metabolism, as the urinary excretion of both nitrogen and sulfur is greatly increased. There was no change in the excretion of sodium, potassium and chloride.

HANSEN, Minneapolis.

STUDIES ON VITAMIN A DEFICIENCY: II. HISTOPATHOLOGY OF SKIN IN HUMAN KERATOMALACIA. M. V. RADHAKRISHNA RAO, Indian J. M. Research **25**:39 (July) 1937.

The changes described consist of superficial hyperkeratosis of the epidermis, extending into the mouths of the pilosebaceous follicles. The sebaceous glands atrophy as do also some of the hair follicles.

SNELLING, Toronto, Canada.

RICKETS: NEW AND OLD PROBLEMS. M. ROHMER, Bull. Soc. de pédiat. de Paris **34**:363, 1936.

This paper presents a concise review of the present knowledge concerning rickets.

BENJAMIN, Montreal, Canada.

THE APPEARANCE OF THE UPPER PART OF THE FEMUR IN RICKETS. S. STEFANINI and GIORGINA GIACOMINI, Lattante **8**:526 (Sept.) 1937.

The upper part of the femur was clinically and roentgenographically studied in 7 rachitic children aged from 1 to 3½ years. The upper part of the femur showed the usual decalcification of the bone and irregularity of the trabecular structure and the epiphysis. There was a tendency for the head of the femur to

be misplaced backward, and the distance between the acetabulum and the upper part of the femur was increased. The angle of the neck of the femur was not obtuse as in normal children but became acute, with resulting coxa vara. The neck of the femur slanted downward, so that it reached below the pubis.

HIGGINS, Boston.

THE ANTISCORBUTIC FACTOR IN CABBAGE. MARIE PODZIMKOVA-RIEGLOVA, Časop. lék. česk. **75**:209 (Feb. 14); 241 (Feb. 21) 1936.

A short review of the literature is followed by charts and graphs showing the antiscorbutic value of several vegetables and of lemon juice. The 1 cc. lemon juice unit is not as definite as the ascorbic acid titer, which was developed after this work was started, and the author will report on the latter in subsequent work. Guinea pigs given scurvy-producing diets were protected against scurvy by the addition of 5 Gm. of raw cabbage daily and by 20 Gm. of sauerkraut even after six months' storage, but were not protected by boiled sauerkraut in quantities up to 40 Gm. a day. This verifies the labile quality of the vitamin C factor in cabbage when exposed to heat. A combination of cabbage and potato is recommended for the diet during late winter and early spring, especially when low cost is of importance.

STULIK, Chicago.

THE ROLE OF VITAMIN C IN INFECTION AND IMMUNITY. H. YU, Chinese M. J. **52**:403 (Sept.) 1937.

This paper gives a good review and discussion of the worldwide literature on the part played by vitamin C in infections of bacterial origin.

NEFF, Kansas City, Mo.

VITAMIN C REQUIREMENT OF INFANTS. K. KAWASHIMA, Acta pædiat. japon. **43**:906 (June) 1937.

In newly born infants and in infants from 2 to 7 months of age the daily vitamin C requirement was estimated as the amount representing the difference between the quantity fed and that which is excreted. According to this method of study, the daily requirement for the average healthy infant during the period of observation was 2 mg. of ascorbic acid.

KATO, Chicago.

THE RELATION BETWEEN INTAKE AND EXCRETION OF ANEURIN (VITAMIN B_1) IN NORMAL MEN. H. G. K. WESTENBRINK and J. GOUDSMIT, Nederl. tijdschr. v. geneesk. **81**:4056 (Aug. 21) 1937.

The excretion of aneurin in relation to the intake by normal subjects was studied by determining the aneurin content of urine by the thiochrome method. With a normal diet, from 70 to 300 micrograms of aneurin was excreted in twenty-four hours. The excretion was increased rapidly to about 600 micrograms in twenty-four hours by the ingestion of 3 mg. of pure aneurin. About 15 per cent of this dose was found in the urine of the first twenty-four hours; no increased excretion was observed in the next period of twenty-four hours. The same results were obtained with ingestion by mouth or by intramuscular injection. When the twenty-four hours was divided into seven periods, in relation to the three chief meals and the time of sleeping, a distinct maximum of the aneurin excretion was found after dinner. During the night a relatively large amount was excreted; the smallest amount was excreted in the morning after breakfast. A large excretion between breakfast and lunch was obtained by the ingestion of 1 mg. of aneurin after breakfast. The authors suppose that a rapid clinical test may be carried out in this way.

VAN CREVELD, Amsterdam, Netherlands.

Hygiene; Growth and Nutrition; Public Health

MATERNAL MORTALITY IN ERIE COUNTY, N. Y. (REPORT OF A SURVEY BY THE MATERNAL MORTALITY SURVEY COMMITTEE OF THE ERIE COUNTY MEDICAL SOCIETY), M. ISRAEL, New York State J. Med. **37**:1479 (Sept. 1) 1937.

This enlightening and instructive report is written by a pediatrician who acted as the chairman for a large committee from the Erie County Medical Society. The fact that the maternal death rate of Buffalo was double that of Rochester, N. Y., in 1932 and that Buffalo had the highest rate of cities of over 50,000 population in the state of New York led to this exhaustive study. The report covers a period from June 1, 1935, to Aug. 31, 1936, and has to do with 12,747 births. A statistical analysis is presented.

Outstanding is the fact that 22.1 per cent of all deliveries were instrumental, 10.3 per cent were by major operative procedure, 7.2 per cent by version and extraction and 3.1 per cent by cesarean section.

"Neonatal mortality rates following version deliveries are significantly higher than those following normal and low forceps deliveries; those following cesarean sections are significantly higher than those following normal, or low or mid forceps deliveries.

"In general, major operative technics lead to a significantly greater chance of immediate death to the offspring than do normal and simpler instrumental technics; while the chances of survival of malplaced fetuses are the smallest of all."

The committee has drawn up outlines for minimal standards of nursing and obstetric care. It criticizes the acceptance of incomplete reports by the health bureau.

"If the certificates continue to be filed without investigation we can see no particular use for Department of Health records, as they do not represent the accurate state of affairs."

Practically no autopsies were performed in cases under the control of the medical examiner.

The analysis clearly shows the danger of cesarean section and of version and extraction. The public should be educated as to the dangers from (1) failure to cooperate with obstetricians, (2) failure to obtain prenatal care, (3) abortions and (4) painless child birth at unwarranted risks.

One large hospital in Buffalo has already ruled that consultations are to be held in all abnormal cases and before any operation of greater extent than the application of low forceps.

AIKMAN, Rochester, N. Y.

PREVENTION OF DISABILITY. A SYMPOSIUM: PREVENTION THROUGH PERIODIC OBSERVATION. M. G. PETERMAN, Wisconsin M. J. **36**:895 (Nov.) 1937

The public and the pediatrician believe in periodic examination, yet the family doctor is the last to become interested. The newborn infant is usually turned over for nursing care with no initial examination. As there is only about forty-eight hours to improve the expansion of an atelectatic lung, early initial observation is indicated. Since some congenital defects (e. g., clubfoot or dislocated hip) need prompt care, the need for early examination is emphasized.

Monthly examinations the first year are advised for recording the weight and other measurements, consideration of the diet and immunization.

Immunization against pertussis (Sauer) is done between the third and the sixth month, against smallpox the seventh and against diphtheria the ninth, with a Schick test in the tenth or eleventh month.

The second year reexaminations are made every three months and urinalyses every six months. Defects in posture are corrected, and the hemoglobin is determined.

By the fifth year a Mantoux test is done. Immunization against scarlet fever is opposed.

An outline for the first year's feeding, examinations and immunizations is given. The general practitioner is neglecting both opportunity and duty in not immunizing the child and making periodic health examinations.

JANNEY, Wauwatosa, Wis.

THE NEW ARGENTINE LAW FOR THE WELFARE OF MOTHERS AND INFANTS. G. ARÁOZ ALFARO, Bol. Inst. internac. am. de protec. a la infancia **11**:239 (Oct.) 1937.

In commenting on the new law for the welfare of mothers and infants, the author recalls the memory of Dr. Emilio R. Coni and Dr. Antonio Vidal as pioneers in the movement toward the creation of a leading and coordinating organization for the protection of children.

The new law establishes the fundamental principle that every child that is born, every mother and every prospective mother remain under the tutorship and supervision of the state. Among the important precepts of the law, the one charging the mother with the duty of feeding her own child and forbidding her to feed any other until her own is 5 months old stands foremost.

The regulation of the new law sets forth the authority of the officers of direction over such important questions as: eugenics, obstetric care, milk control, prohibition of selling alcohol and tobacco to minors and children's attendance at cinemas.

FROM EDITOR'S SUMMARY.

NUTRITION AT THE INFANTS' CLINIC OF THE INSTITUTE OF PEDIATRICS AND CHILD CARE DURING THE LAST THREE FIVE-YEAR PERIODS. M. ACUÑA and J. A. ONETO, Bol. Inst. internac. am. de protec. a la infancia **11**:250 (Oct.) 1937.

Acuña and Oneto make a detailed analysis of the results obtained with methods of feeding during sixteen years. The number of children registered between birth and 12 months of age was 10,246; in the first five year period, 69 per cent of these children were breast fed; in the second period, 70 per cent, and in the third period, only 53 per cent. A mixed feeding was given to 20 per cent of the children in the first period, to 16 per cent in the second and to 26 per cent in the third. The corresponding figures for artificial feeding were 11, 13 and 21 per cent.

FROM EDITOR'S SUMMARY.

HYGIENIC, ECONOMIC AND SOCIAL IMPORTANCE OF PROFESSIONAL GUIDANCE IN BUENOS AIRES, ARGENTINA. DA LEOPOLDO MATA, Bol. Inst. internac. am. de protec. a la infancia **11**:288 (Oct.) 1937.

The following recommendations have been made to the Pan-American Congress concerning the child: 1. Scientific professional guidance controlled by the state should be established in every country as a complement of primary teaching.

2. Applicants for admission to the secondary schools and to the university should be selected according to the results of examinations made by the staff for professional guidance. The same criterion should be adopted by all countries in the distribution of public offices.

3. Laws should be secured allowing adequate teaching of gifted children, classified after a professional guidance examination.

FROM EDITOR'S SUMMARY.

Newborn

METABOLISM AND EXCRETION OF BILE PIGMENT IN ICTERUS NEONATORUM. S. G. ROSS, T. R. WAUGH and H. T. MALLOY, J. Pediat. **11**:397 (Sept.) 1937.

Investigations were conducted on newborn infants to elucidate the causation of icterus neonatorum. The average amount of blood destruction in jaundiced infants is essentially the same as in nonjaundiced infants though it varies

considerably in individuals in both groups. In neither group did the bile pigment in the blood give the prompt direct reaction with the van den Bergh reagent. In almost all infants showing jaundice the indirect (quantitative) van den Bergh reaction showed 5 units or more of bilirubin whereas only a few of the patients without jaundice showed more than 5 units.

Bilirubin was present in the urine of practically all patients with jaundice and was absent in that of practically all patients without jaundice. It appears to depend on the level of bile pigment in the blood rather than on the presence of a promptly reacting pigment.

Studies on the excretion of bile pigment in the stools during the first week of life showed high values for urobilin and bilirubin. In the jaundiced patients the average total excretion was lower than in those without jaundice. Studies on the excretion of urobilin and bilirubin in the urine in the same group of patients showed the average total urobilin excretion to be lower in patients with jaundice than in the nonjaundiced group. Bilirubin was present in measurable quantities in all cases of jaundice. In the cases in which no jaundice was observed, it was nearly always absent.

From this evidence it appears that obstruction of the bile channels plays no part in the production of icterus neonatorum. The jaundice seems to depend on two factors: The first and basic factor is the excessive hemolysis and resultant increase in circulating bile pigment which take place in varying degree in all newborn infants. There does not appear, however, to be unusually excessive hemolysis in the blood of the infants in whom jaundice develops. In these infants there appears to be some factor preventing excretion of the bile pigment. It may be an increased affinity of certain tissues for bile pigment or, more likely, a temporary functional inability of the liver cells to excrete the pigment. Histologic support for this thesis has been observed. The prevalence of jaundice in premature infants may be due to their immaturity and to the consequent functional disturbance of the liver cells.

RAUH, Cincinnati.

PROGRESSIVE BIRTH PALSIES. L. FREEDOM, M. Clin. North America **21**:1387 (Sept.) 1937.

The term "cerebral birth palsy" is a generic one. The condition is characterized by three groups of symptoms: palsy, mental manifestations and epilepsy. By "palsy" is implied a motor deficit involving either the pyramidal tracts, resulting in pareses or plegias, or the extrapyramidal pathways, leading to such manifestations as chorea and athetosis. The mental picture varies from normal through slight diminution of the intelligence to complete amentia. Grand mal seizures occur in about 60 per cent of all cases.

Freedom describes a type of cerebral palsy which is not static but progressive. He has observed, over a period of years, such changes as an involvement of the basal ganglion pathways superimposed on a disorder of the pyramidal tracts, mental retardation and the development of convulsive disorders. These evidences of clinical activity indicate the possibility of a degenerative process involving the cortex and deeper lying structures, but unfortunately they do not reveal the nature of the underlying pathologic developments. They do, however, eliminate from the etiologic background of these progressive lesions such factors as trauma, hemorrhage and maldevelopment.

EUGENE H. SMITH, Ogden, Utah.

THE ANATOMY OF THE SUPERIOR LONGITUDINAL SINUS OF THE NEWBORN. M. JAHIER, Bull. Soc. d'obst. et de gynéc. **26**:651 (Oct.) 1937.

Jahier recommends that the posterior instead of the anterior fontanel be used for puncture of the superior longitudinal sinus in the newborn. He states that the superior longitudinal sinus in 2 cases of 3 is a little to the right of the midline of the posterior angle of the anterior fontanel. On the other hand, the sinus always lies immediately beneath the lambda and is much larger in diameter here than at the posterior angle of the anterior fontanel.

GLASER, Rochester, N. Y.

FAMILIAL ICTERUS GRAVIS OF THE NEWBORN. H. SLOBOZIANU and V. T. IONESCU, Rev. franç. de pédiat. **13**:336, 1937.

The authors differentiate eight types of this condition: (1) the benign, (2) the common, (3) the late severe familial, (4) the acute, in which death occurs within a few hours after birth, (5) the prolonged, lasting for from twenty to forty days, (6) the hemorrhagic and (7) the early and (8) the late involving the central nervous system. They report a case in which death occurred on the twelfth day. There was involvement of the nuclei of the brain stem. The child's temperature was subnormal throughout, from 35 to 36 C. (95 to 96.8 F.). They conclude that the prognosis depends to a certain extent on the time at which transfusion is instituted. It does not seem to depend on the extent of enlargement of the liver or spleen nor on the intensity of the erythroblastosis.

LESLIE, Evanston, Ill.

ANEMIA IN SOME NEWBORN BABIES. J. B. STALLING-SCHWAB, Maandschr. v. kindergeneesk. **6**:487 (Sept.) 1937.

The author describes primary anemia in 5 newborn babies. The anemia developed between the tenth and twenty-first days after birth. In one child the blood picture was that of an aregenerative anemia; in another one it resembled that of anemia infantum pseudoleukaemica (von Jaksch-Hayem anemia), and in a third one it approached that of congenital erythroblastosis. Among the 5 children were two pairs of twins, one pair being infants from a mother who during pregnancy had suffered from the so-called pernicious anemia of pregnancy. All 5 infants got well again and grew up as normal children. The therapeutic measures included intramuscular injections of blood and administration of liver preparations and of reduced iron.

VAN CREVELD, Amsterdam, Netherlands.

Acute Contagious Diseases

VISCERAL PATHOLOGY IN MEASLES: A CLINICO-PATHOLOGIC STUDY OF ONE HUNDRED FATAL CASES. J. A. DEGEN JR., Am. J. M. Sc. **194**:104 (July) 1937.

Of 100 autopsies following measles which disclosed gross and microscopic pathologic changes, 60 per cent concerned children between the ages of 6 and 24 months. Pneumonia, laryngitis and encephalitis were early complications. Death usually occurred in the second and third weeks. The hemolytic streptococcus was the chief organism found bacteriologically at autopsy. No lesion definitely pathognomonic of measles was found.

HENSKE, Omaha.

VISUAL SEQUELAE FROM EPIDEMIC MENINGOCOCCUS MENINGITIS. P. HEATH, Am. J. Ophth. **20**:401 (April) 1937.

A study was made to determine clinical residue persisting in epidemic meningococcic infection, especially relating to the visual system, and to compare these findings with other complications, particularly aural. A complete summary of the medical, neurologic, ophthalmic and otologic examinations of 68 patients selected because of a high proportion of complications is given.

W. S. REESE. [ARCH. OPHTH.]

STUDIES ON HEMOLYTIC STREPTOCOCCI: IV. STREPTOCOCCUS SCARLATINAE. A. C. EVANS, J. Bact. **34**:21 (July) 1937.

Evans has made an extensive study of hemolytic streptococci, and from a collection of 395 strains of hemolytic streptococci from various human diseases she has found 14 strains, all from patients with scarlet fever, which are distinguished from Streptococcus pyogenes by lack of ability to ferment salicin. The group is described in this paper, and from a review of the literature she concludes that the

logical designation for it is Streptococcus scarlatinae. The data show that these strains may cause scarlet fever or sore throat without rash but that rarely, if ever, do they cause other diseases. They are weak in their ability to dissolve human fibrin.

STOESSER, Minneapolis.

LYMPH NODES AS A SOURCE OF NEUTRALIZING PRINCIPLE FOR VACCINIA VIRUS. P. D. MCMASTERS and J. G. KIDD, J. Exper. Med. **66**:73 (July) 1937.

McMasters and Kidd have given some good evidence that every intradermal injection is truly intralymphatic. Dyes introduced in this way enter the superficial plexus of lymphatics through channels torn by the needle; particulate substances which are introduced into the skin by puncture, scratch or even "vaccination" pass in some part directly into these channels and are carried to the regional nodes. Torn lymphatic capillaries remain open for hours, whence it follows that infectious agents introduced by way of a skin wound may reach the lymphatic glands directly. All this being the case, the possibility suggests itself that lymph nodes may do more in defense of the body than act as barriers in the way of invading organisms. Recent work demonstrated the formation of specific bacterial agglutinins in lymph nodes draining the ears of mice into which killed cultures of bacteria had been injected intradermally. Experiments have now been carried out to determine whether lymph nodes of rabbits elaborate a neutralizing principle effective against vaccine virus draining to them.

The data from the experiments prove that regional lymph nodes do elaborate an antiviral principle when virus is brought to them by way of the lymphatics from the ear receiving the injection and that this is demonstrable within four days after the injection of the virus. The immunity following clinical vaccination may in great part have its origin in lymph nodes.

KNICKERBOCKER, Dallas, Texas.

MUTUAL MULTIVALENCE OF TOXIN AND ANTITOXIN. H. EAGLE, J. Immunol. **32**: 119, 1937.

In the presence of an excess of toxin, diphtheria antitoxin binds more of the toxin than would be expected by its neutralizing ability, and the resulting compound is toxic. In the presence of an excess of antitoxin, the toxin combines similarly with more than the neutralizing quantity of antitoxin, and the resulting compound is antitoxic. The precisely neutral compound is formed only in the presence of certain definite quantitative proportions of the two reagents. The observations are in better agreement with the hypothesis of Bordet on the toxin-antitoxin reaction than with the hypothesis of Ehrlich or Arrhenius and Madsen. Both reagents seem multipotent with respect to each other.

I. DAVIDSOHN. [ARCH. PATH.]

THE TREATMENT OF ACUTE POLIOMYELITIS BY INTRAVENOUS INJECTION OF HYPOTONIC SALT SOLUTION. GEORGE M. RETAN, J. Pediat. **11**:647 (Nov.) 1937.

Retan recommends the following procedure in the treatment of anterior poliomyelitis: The patient is placed on a Bradford frame; a lumbar puncture is done, and not more than 7 cc. of cerebrospinal fluid is removed for laboratory examination. The stylet is replaced in the needle, and the needle is left in place, protruding through a window in the frame. An intravenous injection of 0.375 per cent solution of sodium chloride is then given for a period of five hours. This dilution was chosen because it does not produce hemolysis of red blood cells. As many as six or seven intravenous treatments may be necessary, depending on the cell count, the temperature and changes in the reflex picture. The interval between the first and the second treatment must not exceed four hours, nor that between the second and the third treatment, six hours. The intervals between subsequent treatments may be increased, depending on the severity of the disease.

Twelve hours after completion of the third treatment the spinal fluid should be examined; if the cell count is above 20 and if polymorphonuclear cells are present, further treatment must be given. The rate of intravenous flow should be 10 cc. per pound of body weight per hour for the first three hours and somewhat less for the subsequent two hours. To prevent increase in intracranial pressure, the nurse in charge should remove the stylet from the needle at intervals of one-half hour and remove a small amount of cerebrospinal fluid, the amount depending on the rate of flow. Headaches developing during treatment are usually the cause of a lowered intracranial pressure from drainage of too much cerebrospinal fluid.

Contraindications to this form of treatment are: block causing obstruction to the circulation of cerebrospinal fluid; inflammation of the lungs or bronchi; acute nephritis or cardiac weakness, and pyuria or colitis.

Retan reports the results obtained in 57 cases of anterior poliomyelitis in which this method of treatment was used. There were 10 cases of respiratory paralysis in all of which the patients recovered. Six patients with paralysis of deglutition were treated, and all recovered; in fact, they were able to drink fluids after the first treatment. Patients with weakness of the muscles of the extremities without actual paralysis improved promptly. Actual paralysis of the muscles of the extremities did not improve, but treatment of such conditions (if still active) is advised with the hope of preventing further loss of function. Of the patients treated who did not have paralysis, this condition developed in only 3.

RAUH, Cincinnati.

IMMUNIZATION AGAINST THE COMMON DISEASES OF CHILDREN. W. BRYANT RICHARDS, Minnesota Med. **20**:579 (Sept.) 1937.

Richards outlines clearly and concisely the present status of immunization against smallpox, diphtheria, scarlet fever, pertussis, measles, poliomyelitis, chickenpox, mumps, typhoid, tetanus and rabies. Some of the recent literature on these subjects is reviewed. This is a well written and excellent article for both the general practitioner and the pediatrician.

ANDERSON, Minneapolis.

CONGESTIVE HEART FAILURE IN WHOOPING COUGH. A. R. THOMPSON, Brit. J. Child. Dis. **34**:273 (Oct.-Dec.) 1937.

A 4 year old girl had whooping cough complicated by bronchopneumonia and an unusual degree of congestive cardiac failure proceeding to general anasarca. There was no evidence of previous cardiac disease; however, there was a history of faucial diphtheria eight months before.

The urinary output diminished steadily. Digitalis and finally two suppositories containing mercury were resorted to, with considerable improvement in the child's general condition and with effective diuresis.

Some investigators maintain that apart from cardiac dilatation during the paroxysmal stage there are some instances in which the attack has left permanent damage and even valvular disease. Others agree that a temporary mechanical strain may occur, affecting more particularly the right side of the heart, but they have failed heretofore to find permanent damage either of the myocardium or of the endocardium.

LANGMANN, New York.

THE COMBINING PROPERTIES OF VACCINIA VIRUS WITH THE ANTIBODIES DEMONSTRABLE IN ANTIVACCINIAL SERUM. M. H. SALAMAN, Brit. J. Exper. Path. **18**:245, 1937.

The hypothesis is tentatively advanced that neutralization of the virus by antivaccinial serum depends on an antibody distinct from those responsible for agglutination and precipitation. FROM THE AUTHOR'S SUMMARY. [ARCH. PATH.]

EFFECT OF ASCORBIC ACID (VITAMIN C) ON TOXIN PRODUCTION BY CORYNEBACTERIUM DIPHTHERIAE. I. J. KLIGLER, L. LEIBOWITZ and M. BERMAN, J. Path. & Bact. **45**:415, 1937.

The addition of from 0.05 to 0.1 per cent ascorbic acid to culture medium suitable for the production of toxin by Corynebacterium diphtheriae renders filtrates of such cultures less toxic. The toxicity of vitamin-containing filtrates is only about one twentieth of that of control cultures. The ascorbic acid is rapidly oxidized in the culture medium at a temperature of from 30 to 37 C., but in the presence of bacterial growth it is preserved longer than in sterile medium. Glutathione, another potent biologic oxidation-reduction agent, has no effect on the toxicity of cultures. Small amounts of ascorbic acid (from 0.1 to 0.2 per cent) mixed with toxin in a test tube and incubated at 30 C. render the toxin atoxic in from two to three days according to the concentration of the vitamin. This reaction occurs under both aerobic and anaerobic conditions. Contrary to the findings in growing cultures, the ascorbic acid disappears more rapidly in the toxin filtrate than in sterile medium. Toxin injected into guinea pigs leads to a rapid decrease in the vitamin C content of the adrenal glands. When a lethal dose of toxin is given, the vitamin C content may be reduced to nil. It is suggested that the ascorbic acid destroys the toxin by an oxidation-reduction reaction and that the action is similar to that produced by aldehydes in general.

FROM THE AUTHORS' SUMMARY. [ARCH. PATH.]

PERTUSSIS ENDOTOXIN IN THE TREATMENT OF WHOOPING COUGH. A. R. THOMPSON, Lancet **2**:733 (Sept. 25) 1937.

Treatment with an endotoxin extract of Haemophilus pertussis appeared to be of most value when begun in the catarrhal or early paroxysmal stage of the disease, before the onset of whooping.

Pertussis endotoxin was found capable of eliciting focal reactions with exacerbation in symptoms when given to certain subjects suffering from whooping cough. Even though this reaction may be followed by improvement, it was thought to constitute a contraindication to the employment of this treatment in very young subjects.

LANGMANN, New York.

VACCINATION AGAINST TYPHUS. J. LAIGRET, R. DURAND, J. BELFORT and J. LEFAUCHEUR, Arch. Inst. Pasteur de Tunis **26**:453, 1937.

In this report of 170 pages are presented the results of vaccinating 32,481 persons against exanthemic typhus with an "enrobed" living vaccine (a rat brain suspension "enrobed" or coated with egg yolk and oil), previously described (ibid. **25**:570, 1936). The usual result of the vaccination was an inapparent infection, although in 5 cases mild typhus followed the vaccination within from ten to sixteen days. These attacks occurred in Europeans, the vaccination of whom was regarded as entailing a light risk. Both vaccination and delousing thus far are recommended. Epidemiologic evidence indicates that definite immunity has been induced.

M. S. MARSHALL. [ARCH. PATH.]

VARICELLA AFTER CONTACT WITH HERPES ZOSTER. M. MORO, Bull. Soc. de pédiat. de Paris **35**:122 (Feb.) 1937.

A boy aged 1 year had varicella sixteen days after his grandmother had herpes zoster on the right side of the thorax. He was acutely ill, and recovery was interrupted by bilateral suppurative otitis media. It is pointed out that varicella following exposure to herpes zoster is not uncommon, while the reverse is rare.

BENJAMIN, Montreal, Canada.

CLINICAL PICTURE OF EPIDEMIC CEREBROSPINAL MENINGITIS. A. VERITTI, Lattante **8**:172 (April) 1937.

The 13 cases of meningococcic meningitis seen in the pediatric division of the city hospital of Udine, Italy, during the last two years are listed and classified. Five patients died, and 8 recovered.

HIGGINS, Boston.

SERUM TREATMENT FOR POSTDIPHTHERITIC PARALYSIS. G. FILECCIA, Lattante **8**:176 (April) 1937.

Two children with postdiphtheritic paralysis were treated with large doses of antitoxin; one child received 200,000 units and the other 100,000 units, 20,000 units being given daily. To prevent anaphylactic reactions, injections of calcium were given. Excellent clinical results are claimed for this method of treatment.

HIGGINS, Boston.

POLIOMYELITIS WITH MENINGEAL AND SPASTIC SYMPTOMS. O. BIZZARRI, Lattante **8**:178 (April) 1937.

A case of poliomyelitis is reported, in which the meningeal symptoms predominated.

HIGGINS, Boston.

THE FREQUENCY OF POSTSCARLATINAL NEPHRITIS IN EARLY CHILDHOOD. R. R. RAPPOPORT, Pediatria, 1937, p. 50.

The incidence of postscarlatinal nephritis is much smaller for children under 3 years of age than for older children. This is attributed to differences in the cardiovascular development. The arteries are said to be wider in infants, beginning to narrow at about 2 years of age, reaching a minimum at about 18 years and thereafter widening. The low blood pressure in early childhood is attributed to the apparently greater width of the capillaries and arteries.

MCKHANN, Boston.

HEINE-MEDIN'S DISEASE. EDGAR FILGUEIRAS, J. de pediat., Rio de Janeiro **4**:458 (Oct.) 1937.

The diagnosis, clinical forms and treatment of poliomyelitis are discussed.

SANFORD, Chicago.

ETIOLOGY OF SCARLET FEVER. F. V. BORMANN, Ergebn. d. inn. Med. u. Kinderh. **50**:243, 1936.

In reviewing the investigations on the etiology of scarlet fever the author comes to the following conclusions:

1. One can obtain hemolytic streptococci in pure culture at the portal of entry of the infection in 100 per cent of all cases of beginning scarlet fever. They appear at the onset of the disease and toward the period of convalescence are usually replaced by bacteria that normally abound in the throat. The hemolytic streptococci are found with such a constancy in almost pure culture in the pus obtained from persons with complications of scarlet fever that one is forced to consider them the etiologic agents. Whenever bacteria are found in the organs of a patient with scarlet fever or whenever the blood culture is positive, the organism found is usually the hemolytic streptococcus. Also, the surroundings of the patient, the human beings as well as inanimate objects, are tainted with hemolytic streptococci to an unusual degree.

2. The introduction of pure cultures of hemolytic streptococci, obtained from patients with scarlet fever, into the throats of persons susceptible to scarlet fever induces a typical attack of the disease.

3. The scarlatina streptococcus is not only capable of producing an exotoxin, as is the diphtheria bacillus, but like most other streptococci it gives rise to widespread pyogenic and septic processes. The exotoxin brings about the "typical" syndrome of scarlet fever, with initial intoxication, enanthem, exanthem, fever, vomiting and headache. In the second half of the first week, the streptococci proper invade the organism, causing a secondary infection with pyogenic complications. In the second to third week of the disease, the poisoning by exotoxins subsides and there is established an antiexotoxin immunity, as evidenced by negative results from a Dick test and the blanching capacity of the blood. This immunity lasts, as a rule, a lifetime. The intoxication primarily prepares the soil for the invasion of the patient's body by the streptococci. Various pyogenic complications and nephritis are the sequelae of the invasive activity of the streptococci. Only in the fifth or sixth week of the disease is this danger averted, at a time when the antibacterial lytic bodies appear in the patient's blood stream. This antibacterial immunity, like any other typical streptococcic immunity, lasts only a short time. Persons immune to scarlet fever are therefore permanently protected against the toxic, but not the pyogenic, manifestations of the producers of scarlet fever. Dick toxin behaves in all its immunologic and clinical phases purely as an exotoxin.

CAPPER, Philadelphia.

MILIARIA SCARLATINOSA SUPPURATIVA. G. LIEBMANN, Med. Klin. **33**:1368 (Oct. 1) 1937.

Three cases in which a finely pustular eruption developed on the basis of the scarlet fever exanthem are reported. In 1 case streptococci were yielded by a culture of the contents of the pustule; in the other 2 the cultures consisted of benign pus-producing organisms. The condition is apparently uncommon. It may be a manifestation of infection of sweat glands damaged by scarlet fever toxin.

SIEMSEN, Chicago.

GERMAN MEASLES AND TUBERCULIN REACTION. E. SLAWIK, Med. Klin. **33**:1640 (Dec. 3) 1937.

Although in general German measles is much milder than measles, differential diagnosis may be difficult. Slawik observed a child in whom the Moro reaction to tuberculin was strongly positive and in whom German measles developed twelve days later. Although the site of reaction had faded completely, it was reactivated by German measles. Fine, dark red papules made the area stand out from the less intensely red exanthem. Since the influence of measles on the tuberculin reaction is opposite to that of German measles, the latter disorder must be regarded as a distinct entity.

SIEMSEN, Chicago.

INFANTILE PARALYSIS WITHOUT PARALYSIS: ABORTIVE FORM OF MENINGITIC POLIOMYELITIS. E. WIELAND, Schweiz. med. Wchnschr. **67**:1105 (Nov. 20) 1937.

Wieland reports that local epidemics of poliomyelitis developed in different parts of Switzerland between the early summer and November of 1936. In all, 1,270 cases were reported by physicians. The clinical and epidemiologic behavior varied greatly, but on the whole the course was unusually benign. In the children's clinic in Basel 26 patients with poliomyelitis were treated, and there was not a single fatality. Nineteen of the patients were hospitalized between the second and the fifth day of the disease, with high fever and symptoms of the so-called meningitic form of poliomyelitis. All these patients recovered completely without paralytic symptoms in the course of several weeks. However, all patients passed through more or less severe muscular weakness, which was preceded by anomalies in the reflexes. Such cases of "infantile paralysis without paralysis," or of the abortive forms of the so-called meningeal type of poliomyelitis, have

been described before, sometimes under the misleading term aseptic serous meningitis. Wieland points out that these cases seem to be everywhere on the increase and thinks that they indicate that the character of epidemics of poliomyelitis is becoming milder. Whether certain noncharacteristic, febrile infections without signs of nervous irritation, which develop in persons who come in contact with poliomyelitic patients (so-called contact cases), belong to the sphere of abortive poliomyelitis has not been definitely decided. It is likewise difficult to estimate whether the surprisingly favorable therapeutic results are due to the benign character of the disease or to the early treatment with convalescent serum, parent's blood and large doses of sodium salicylate. Observations in cases in which the treatment was begun later seem to indicate that both the benign character of the disease and the early onset of the serotherapy were factors in the favorable results. With regard to the control of epidemics of poliomyelitis, Wieland says that in addition to early therapy and isolation of the patient it is important to watch the healthy members of the patient's family, for the virus seems to be transmitted less often by direct contact than by indirect contact through healthy intermediate carriers to susceptible young persons.

EDITOR'S ABSTRACT. [ARCH. NEUROL. & PSYCHIAT.]

PRIMARY DIPHTHERIA OF THE NASAL CAVITY IN CHILDREN. W. GUMINSKI, Pedjatrja polska **17**:23 (Jan.-Feb.) 1937.

Primary diphtheria of the nasal cavity is spread by carriers. It affects children of all ages. The newborn are frequently affected, because the nursing mother may be a carrier of the infection. The disease appears in two clinical forms, mild and severe, depending on the child's resistance.

The disease is highly treacherous; it is often overlooked unless definite symptoms are present. The treatment is prophylactic, general and local. The author particularly emphasizes local treatment.

KRUPINSKI, Chicago.

A RARE OCULAR SEQUELA OF PERTUSSIS. JAN VANYSEK, Časop. lék. česk. **75**:140 (Jan. 31) 1936.

The author reviews the literature and cites the more common ocular complications which follow pertussis, such as hemorrhage in the anterior chamber and in the subscleral, retinal and subretinal areas, with separation of the retina in the last mentioned. A case is reported. A boy aged 11, whose mother died of pulmonary tuberculosis, had tuberculous cervical adenitis at 6 and pneumonia at 9 years. After pertussis rapid loss of vision occurred, and examination showed papilledema of 3 diopters and engorgement and tortuosity of the retinal vessels. The Pirquet reaction was positive. Neurologic examination revealed associated pertussis encephalitis with inflammation of the head of the optic nerve. During convalescence the symptom of euphoria was predominant.

STULIK, Chicago.

STREPTOCOCCI IN CASES OF DIPHTHERIA. A. DOSKOCIL, Časop. lék. česk. **75**:181 (Feb. 7) 1936.

Streptococci seem to multiply more rapidly in cases of diphtheria in which the patient is given antitoxin late or in insufficient doses. This is probably due to the lowered resistance of the mucous membranes as a result of injury caused by diphtheria toxin. Of 16 children studied post mortem, 5 died within five days, 5 within a week and 6 during the second week and the beginning of the third week. The causes of death in various cases were as follows: mediastinal abscess; retropharyngeal abscess; nasopharyngeal hemorrhage, and miliary abscesses of the internal organs, including the myocardium. The important feature of treatment in toxic diphtheria is early and large doses of both antidiphtheria serum and polyvalent streptococcus serum. Frequent transfusions of from 70 to 100 cc. of blood are advised as accessory support.

STULIK, Chicago.

THE FIRST DIAGNOSIS OF DIPHTHERITIC PARALYSIS IN HUNGARY (1860). J. BÓKAY, Orvosi hetil. **81**:757 (July 17) 1937.

In his last article, the famous old Hungarian pediatrician Bókay reports that the first diagnosis of diphtheritic paralysis was made by his father, Bókay Sr., one of the most famous Hungarian pediatricians of his age, in the case of his adopted brother in 1860. At that time the clinical picture had been described only by the American Abraham Jacobi and the French Maingault and Trousseau. Bókay Sr. reported 4 cases in the year 1863. In this report he wrote only about "paralysis in childhood" and remarked that Jacobi and Maingault thought that this clinical picture was caused by diphtheria. The first case was one of progressive paralysis which attacked the respiratory muscles and ended in death.

GÖTTCHE, Budapest, Hungary.

THE MITIGANT EFFECT OF ASCORBIC ACID ON DIPHTHERIA TOXIN. K. FARKAS, Orvosi hetil. **81**:770 (July 24) 1937.

Experiments made on guinea pigs showed that ascorbic acid has an immediate effect on diphtheria toxin. This effect can occur when the ascorbic acid is mixed with the diphtheria toxin in a test tube and then injected into the skin of guinea pigs, and it can occur when the ascorbic acid is given separately a day later or a day earlier in the same tissues where the toxin was or will be given. The effect can be further proved when simultaneously with the injection of the diphtheria toxin, or a little earlier, the ascorbic acid is injected into the peritoneal cavity of the guinea pig. It seems logical that in cases of diphtheria, especially in those of malignant diphtheria, a large amount of ascorbic acid should be injected into the organism, even if nutrition shows a sufficient amount of vitamin C.

GÖTTCHE, Budapest, Hungary.

GASTRITIS DUE TO DIPHTHERIA TOXIN. T. YOKOYAMA, J. Orient. Med. **27**:1 (July) 1937.

Intraperitoneal injections of diphtheria toxin in rabbits and cats were followed first by catarrhal inflammation of the gastric mucosa and later by hemorrhagic ulcers. The ulceration occurred frequently at the cardia but rarely at the pylorus. Such changes are produced primarily by the hematogenous intoxication; they are secondarily aggravated by the acid-digesting juice of the gastric secretion.

KATO, Chicago.

HEMOLYTIC STREPTOCOCCI IN THE PHARYNGEAL MUCOUS MEMBRANES OF PATIENTS WITH SCARLET FEVER. R. ISHIMURA and R. SUGITA, Acta pædiat. japon. **43**:863 (June) 1937.

The observers classified the hemolytic streptococci obtained from the throats of patients with scarlet fever into seven types (A, B, C, D, E, F and G). Types A, B and C are relatively mild, while the remaining types are virulent. The virulent types are associated with a more protracted course of the disease; they are more frequently found in older children and adults and are most prevalent during the colder seasons of the year. In children suffering from scarlet fever at least one of these types of hemolytic streptococci was isolated in 100 per cent of cases.

KATO, Chicago.

PROGNOSIS OF NEPHRITIS IN SCARLET FEVER. E. PETRÉN, Svenska läk.-tidning. **34**:218 (Feb. 5) 1937.

In 1908-1935, 7,140 patients with scarlet fever were treated at the Contagious Hospital of Malmö, Sweden. Of these, 307, or 4.3 per cent, had nephritis, and 12 of these children died (3.9 per cent). The incidence of nephritis varied con-

siderably, from 14.5 to 0 per cent; the average incidence was 4.3 per cent. Of the 295 who were discharged living from the hospital, 17 died later, none from nephritis. Of the remaining 278 persons, 13 could not be found at the time of the examination in 1936; 11 did not give any information about their state of health; 176 were examined; 52 sent specimens of urine; 26 reported their state of health. It turned out that 6 persons had nephritis and that hypertonia was present in 8.

WALLGREN, Göteborg, Sweden.

AN EPIDEMIC OF POLIOMYELITIS. A. NORDENSKJÖLD, Svenska läk.-tidning. **34:** 1051 (July 23) 1937.

The first cases of poliomyelitis occurred in the district of Bohuslän, Sweden, in April 1936. The number increased in May and June; the maximal morbidity occurred in August, then rapidly decreased; the last few cases occurred in January 1937. Altogether, the disease was diagnosed in 315 persons. During the whole year of 1935, only 10 cases were reported in the same district. The youngest patient was 4 weeks old; 6 patients were below 1 year of age. A characteristic feature in this epidemic as in those of later years in Sweden was the high frequency of poliomyelitis among grown-up people. No less than 160 of the patients were more than 15 years of age, with a maximal incidence in those between 15 and 20 years of age. The mortality rate was 11.4 per cent. Eleven of the fatal cases were in children, and the remaining 25 fatal cases were in patients more than 15 years of age. The mortality was thus greater in those who were past childhood. Of the 52 patients who were in a preparalytic stage when first seen, 28 remained without any paralysis. No effect of the treatment with convalescent serum was discernable.

WALLGREN, Göteborg, Sweden.

AN EPIDEMIC OF THE HEINE-MEDIN'S DISEASE IN 1936. J. M. SOETERS, Maandschr. v. kindergeneesk. **7:**29 (Oct.) 1937.

The author presents a short description of 10 cases of Heine-Medin's disease observed in a small Dutch village in 1936. All the patients were young children. There is also a discussion of 3 other typical cases.

VAN CREVELD, Amsterdam, Netherlands.

Acute Infectious Diseases

A STUDY OF BRUCELLA INFECTION AND IMMUNITY IN HUMANS. I. F. HUDDLESON, M. MUNGER, S. E. GOULD and D. PAULSON, Am. J. Trop. Med. **17:**863 (Nov.) 1937.

The authors studied 8,124 persons for Brucella infection and immunity by means of an allergic skin test, the agglutination test and the Brucella opsonic test and by means of blood, stool and urine cultures.

Of the total number examined, 845, i. e. 10.3 per cent, gave a positive cutaneous reaction; 7.1 per cent were classified as infected, 2.7 per cent as immune and 0.52 per cent as questionably immune.

Of the 222 classified as immune, 47.3 per cent gave blood samples that showed insignificant serum agglutination.

Of the 436 classified as infected, 90.5 per cent gave blood samples that showed insignificant serum agglutination.

They concluded that the brucellergin skin test, with use of a 1:25,000 dilution, is the most accurate test for detecting infection with and immunity to Brucella.

BURPEE, Augusta, Ga.

A Study of the Mechanism of the Production of Toxic Substances by the Salmonella Group of Bacteria. F. L. Kraft and C. N. Stark, J. Infect. Dis. **61**:315 (Nov.-Dec.) 1937.

Cultures of Salmonella grown in broth have been shown to produce something in the nature of a heat-stable endoenzyme which, when released by natural autolytic processes or by a brief subjection of the culture to 100 C., is capable of acting on the broth constituents to produce certain changes characterized by a gradual increase in p_H paralleled by an increase in toxicity. The findings reported here indicate that at least a part of the poisonous substances, often called endotoxin, are split products of the culture medium, resulting from the action on that medium of this heat-stable endoenzyme.

Toomey, Cleveland.

Clinical Observations on Grippe as Seen in Pediatric Practice. C. A. Aldrich, J. Pediat. **11**:331 (Sept.) 1937.

Aldrich analyzed his observations on 1,146 patients with grip treated between February 1930 and January 1936. Grip occurred in yearly epidemics, and the epidemics showed no chronologic relation to the prevalence of general respiratory disease in comparison with the incidence of pharyngitis. Laryngitis, or croup, occurred in smaller epidemics identical in time with those of grip, indicating that croup may be a manifestation of grip in infancy. Otitis media and capillary bronchitis were the commonest complications. Seventy per cent of the children in whom capillary bronchitis developed were known to be asthmatic, and another 17 per cent were probably allergic. Aldrich believes that this raises the question whether the physical findings leading to the diagnosis of capillary bronchitis were not due to an allergic reaction in the bronchi. The only death was due to meningitis, which resulted when measles complicated grip with mastoiditis.

Rauh, Cincinnati.

Active Immunization Against Tetanus in Warfare. F. H. Van Wagoner, Mil. Surgeon **81**:365 (Nov.) 1937.

Repeated experiments have shown that active immunization with tetanus toxoid induces a state in which further stimulation with the same antigen causes in the recipient a rapid and persistent rise of tetanus antitoxin to levels which are greatly in excess of those shown after injection of 1,500 units of tetanus antitoxin.

Sanford, Chicago.

The Rheumatic State. A. LeSage, Union méd. du Canada **66**:909 (Sept.) 1937.

Present knowledge of the rheumatic state is entirely different from that of earlier days. Having split off gout, pseudoinfectious arthritis and chronic arthritis, present observers have included the various cardiac forms, pleuropulmonic syndromes, intestinal manifestations, cerebral forms and some of the acute pharyngeal anginas. LeSage summarizes the principal present day beliefs thus:

1. Rheumatism is a microbial infection with a specific organism yet unknown, feebly contagious.

2. Anatomically, it is characterized by Aschoff bodies, which attack the myocardium by election.

3. From the clinical point of view, the cardiac lesions are primary and certain; the joint symptoms, secondary and fleeting.

4. Therapeutically, sodium salicylate acts as a decongestant and antiseptic. Its action, especially antiallergic, is most beneficial for the joints; the action is very weak against the cardiac lesions.

LeSage prescribes salicylate by mouth in this form:

Sodium salicylate	30.0	Raspberry syrup	50.0
Sodium bicarbonate	60.0	Water	100.0
Lactose	10.0		

One teaspoonful contains 1 Gm. of salicylate and 2 Gm. of bicarbonate.

DAFFINEE, Boston.

RHEUMATISM AS A CLINICAL PROBLEM. N. M. FRISCHMANN, Arch. de méd. d. enf. **40**:565 (Sept.) 1937.

In an effort to classify the rheumatic conditions of childhood, Frischmann has developed an elaborate scheme of clinical entities, based on etiologic and morphologic criteria and eliminating the articular manifestations noted in the course of such infections as tuberculosis, syphilis, gonorrhea and scarlatina.

The term "rheumatism" should imply in most cases a chronic process with an undulating evolution, beginning frequently with the phenomena of acute polyarthritis and characterized by a particular inflammatory lesion of the mesenchymal system, with formation of specific Aschoff bodies and with localization of the lesion in the cardiovascular system. There is usually invasion of the synovial membranes, and frequently there is involvement of the serous membranes.

Any practical classification of rheumatic diseases should (1) embrace all forms of rheumatism, including even the rare types, (2) define the stage of the disease in question and (3) show the degree of compensation in the organism, not only in the cardiovascular system but in the body as a whole.

The conclusions reached in this extensive discussion of a subject on which opinions differ so widely are:

1. The theory of a purely local involvement has retarded the progress of studies of rheumatism in children.

2. Rheumatism is not a disease of the organs of locomotion.

3. Acute polyarthritis of independent evolution is always of rheumatic origin.

4. The term "true rheumatism," now accepted in the literature, creates confusion.

5. Rheumatism of childhood is usually a chronic disease, with exacerbations at irregular intervals and with continuing damage. AMESSE, Denver.

AN UNUSUAL ACCIDENT FROM EMETIN IN A BABY. F. LO PRESTI-SEMINERIO, Méd. inf. **8**:350 (Nov.) 1937.

A boy of 1 year who had amebic dysentery and who was given two injections of emetine and coramine (a 25 per cent solution of pyridine betacarbonic acid diethylamide) showed a systemic reaction and local necrosis and died. The family tree was plotted for from three to five generations. The author believes that a hereditary dystrophy was responsible for the severe reaction and death.

HIGGINS, Boston.

INFECTION WITH SCHISTOSOMUM MANSONI. A. DUARTE, J. de pediat., Rio de Janeiro **4**:423 (Oct.) 1937.

This organism, originating in Africa, has become prevalent in northern South America. The symptoms of infection are fever, dysentery, hematemesis, splenomegaly, hepatomegaly, ascites, anorexia albuminuria and eosinophilia. The diagnosis is made on discovery of the parasite. The prognosis is good. The treatment is by combinations of emetine hydrochloride and antimony and potassium tartrate. This is an excellent article. It runs through the November issue of this journal as well. It should be read in detail by those interested.

SANFORD, Chicago.

MANSON'S PARASITE. A. DUARTE, J. de pediat., Rio de Janeiro **4**:515 (Nov.) 1937.

Five cases of infection with this intestinal parasite are discussed in detail. Such infection presents a considerable problem in Brazil, and is widely distributed. The symptoms are chronic diarrhea with progressive enlargement of the abdomen. This is due to ascites and splenomegaly. The treatment is by vermifuges and calcium chloride.

SANFORD, Chicago.

MALARIA IN THE LIGHT OF ALLERGY. P. E. SABLIN, Vrach. delo **19**:519, 1937.

Sablin presents a detailed account of the various types of manifestations which may be observed clinically in the course of malaria and discusses them in terms of allergy. His summary and conclusions are as follows:

"1. Several of the clinical manifestations of malaria may be explained by the development of allergy in the person afflicted with the disease.

"2. The various allergic processes may originate under the influence of the malarial products of cellular disintegration on a sensitized organism.

"3. The allergic processes occurring in the course of malaria may be manifested by several forms: (a) The hyperactive form, with the usual type of response to the malarial infection but exaggerated. These are the characteristic cyclic neurovegetative pathologic reactions which improve rapidly under specific antimalarial treatment. In this form a severe malarial paroxysm may occur in the presence of an almost negligible number of parasites in the peripheral blood. (b) The dysreactive form, with a qualitatively atypical response to the disease. This form comprises the reactions resembling clinically anaphylactic shock, with the occurrence of collapse, which rapidly leads to a fatal termination (malaria perniciosa algida syncopalis). This group also includes the so-called malaria larvata. (c) The areactive form, which is manifested by reactions of an inflammatory and degenerative character in the various organs of the body, such as gastroenteritis and diffuse glomerulonephritis, which do not respond readily to specific antimalarial therapy and which lack the cyclic character of malarial manifestations.

"For the establishment of a rational form of therapy, one which would take into consideration the state of reactivity of the organism, it is necessary to differentiate between the aforementioned atypical manifestations of malaria.

"For the hyperactive and dysreactive forms of malaria the specific antimalarial treatment should be supplemented with desensitization by foreign protein therapy and other treatment, while for the areactive form, which does not respond readily to the specific treatment, a stimulating form of therapy (physical therapy) should be used, with recognition of the existing contraindications."

BODER, Los Angeles.

SEPSIS CAUSED BY BACILLUS PYOCYANEUS. J. M. SOETERS, Maandschr. v. kindergeneesk. **7**:74 (Nov.) 1937.

Soeters gives an extensive description of sepsis in a girl of 1½ years, caused by Bacillus pyocyaneus. She showed a specific involvement of the skin known in literature as ecthyma gangraenosum. He also gives a short description of a baby with chronic cystitis from whose urine, during four months after infection with Bacillus coli, without clinical symptoms, B. pyocyaneus could be cultivated.

VAN CREVELD, Amsterdam, Netherlands.

AN EPIDEMIC OF CATARRHAL JAUNDICE. C. DEN HARTOG, Nederl. tijdschr. v. geneesk. **81**:4363 (Sept. 11) 1937.

This is a description of an epidemic of so-called catarrhal jaundice. In an area 10 kilometers square over 200 patients were observed. Forty-one cases

observed by the author are described somewhat in detail. The period of incubation was found to be from two to four weeks.

VAN CREVELD, Amsterdam, Netherlands.

TAME WHITE RATS AS A SOURCE OF INFECTION WITH THE LEPTOSPIRAE OF WEIL'S DISEASE. G. KORTHOF, Nederl. tijdschr. v. geneesk. **81**:4571 (Sept. 25) 1937.

Korthof reports Weil's disease in a laboratory worker who looked after tame white rats but did not swim nor have any contact with wild rats. He had not been bitten by the rats. The most simple and reliable method to detect this infection in white rats appeared to be by examination of the blood for agglutinins against the leptospirae of Weil's disease. For isolating the leptospirae culturing kidney material under due precautions was more simple and reliable than inoculating guinea-pigs.

VAN CREVELD, Amsterdam, Netherlands.

Chronic Infectious Diseases

FACTORS INFLUENCING THE COURSE OF TUBERCULOUS INFECTION IN YOUNG CHILDREN. M. BRAILEY, Am. Rev. Tuberc. **36**:347 (Sept.) 1937.

A series of 223 children (91 white and 132 colored) have been followed for periods ranging from one to eight years. All had had an examination before the second year of age; all reacted positively to tuberculin; all had had a roentgen examination of the chest and had been under observation for at least one year, unless death had intervened at the time of writing. At the initial roentgen examination, 94 showed parenchymal involvement, and 129 showed no definite lesion. Of the former, 28 per cent died during the first year. After the first year no deaths occurred among the white children, but additional deaths raised the eight year mortality for the colored children to 47 per cent. As to the children with no roentgen evidence of lesions, none among the white children died during the first year, but 7 per cent of the colored children died. At the end of eight years the mortality for the white children of this group was less than 2 per cent, and that for the colored children, 12 per cent. The first year of known infection was the most dangerous; more than three fourths of the mortality among white children and one half of that among colored children fell within this period. Also, the mortality from tuberculosis was almost twice as high in infants known to have been infected before the sixth month of age as in those whose infection was discovered between the sixth month and the end of the second year. The immediate cause of death was almost always tuberculous meningitis or generalized tuberculosis.

EUGENE H. SMITH, Ogden, Utah.

TREATMENT OF SYPHILIS IN INFANTS. H. M. ROBINSON, M. Clin. North America **21**:1397 (Sept.) 1937.

A rational system of treatment of syphilis in infants may be planned under the following heads:

1. Preventive (prenatal care and treatment)
2. Curative (in early congenital or acquired syphilis)
3. Arrestive (in late tardive congenital syphilis)
4. Supportive

The supreme method of treating congenital syphilis is to prevent it, and with modern methods a healthy infant is the rule if treatment of the mother is begun between the fifth and sixth months.

To accomplish a cure in early congenital syphilis it is necessary to detect its presence early, before the age of 2 months. A definite diagnosis should be a prerequisite of treatment, and in the final analysis the infant's blood is the most

reliable indicator as to the presence or absence of the disease. Treatment begun at this early date and continued over a period of twenty-four months will insure a cure in a large proportion of cases. Arrestive treatment is less satisfactory but should be continued for one and a half years. At the end of this time the serologic observations are almost invariably positive. Further treatment should be given every one, for two or three years.

As regards supportive treatment, children with late congenital syphilis who have destructive lesions in the cornea and nervous system require other than antisyphilitic measures and come within the domain of the ophthalmologist and that of the neurologist.

The author's preference as to drugs and his methods of treatment are described fully.

EUGENE H. SMITH, Ogden, Utah.

THE EGG AS A MEDIUM FOR CULTIVATION OF MYCOBACTERIUM TUBERCULOSIS FROM TUBERCULOUS MATERIALS. G. I. WALLACE and M. R. WEISSBUCH, Proc. Soc. Exper. Biol. & Med. **37**:304 (Nov.) 1937.

The shells of fresh and hard-boiled eggs were sterilized with 5 per cent phenol followed with 95 per cent alcohol. They were then pierced with a sterile pin. Sputum was concentrated with 6 per cent sulfuric acid, 3 per cent hydrochloric acid, 4 per cent sodium hydroxide and 5 per cent oxalic acid, and the residue after concentration was injected in inoculums of 0.5 cc. into the eggs. The eggs were then placed in the incubator at 37 C. for twenty days. At the end of the period of incubation they were broken and the contents placed in Petri dishes. In both the whites and the yolks there were easily visible numerous grayish patches, which were not present in the control eggs. When the grayish patches were picked out, crushed on a glass slide and stained by an acid-fast procedure, they disclosed countless numbers of acid-fast rods. When material from the eggs showing infection was inoculated into guinea pigs it produced active tuberculosis in all. Seven of 8 raw eggs and 6 of 8 hard-boiled eggs gave definitely positive growths when inoculated with concentrated sputum. Acid-fast organisms also could be found in abundance in ten days, although the growths were not as marked.

HANSEN, Minneapolis.

ARTIFICIAL PNEUMOTHORAX IN CHILDREN. C. D. S. AGASSIZ, Tubercle **19**:74 (Nov.) 1937.

The hopeless attitude so commonly assumed in regard to the prognosis of pulmonary tuberculosis in childhood is without justification if modern methods of treatment are instituted at the proper time. True, the progress of the disease is usually rapid and, if not arrested, soon terminates fatally. Agassiz' more extended experience with artificial pneumothorax has now led him to advise a wider application of this measure than he formerly considered warranted, both earlier and later in the course of the disease. Time, however, is an especially important factor in tuberculosis in children, and delay in the institution of compression therapy when such therapy is indicated may lead to failure.

Certain conditions that are important in adults do not have the same significance in children. Adhesions are probably not so dense in the young, and the presence or absence of cavitation is not of great importance in deciding whether pneumothorax should be used or not. The toxemia is the principal cause of the child's symptoms, and if it is possible to reduce this factor by putting the lung at rest, an attempt to do so is justified. As to complications, some effusion of fluid occurred in from 30 to 50 per cent of Agassiz' cases. He now believes that this is possibly of benefit, and no attempt is made to remove the fluid unless it becomes large in amount.

The recovery from seemingly hopeless disease following the institution of artificial pneumothorax is the justification of the author's optimism.

EUGENE H. SMITH, Ogden, Utah.

THE EHRLICH, WEISS, PETZETAKI AND DE SILVESTRI REACTIONS IN TUBERCULOSIS OF CHILDREN. M. BATTISTA, Méd. inf. **8**:320 (Oct.) 1937.

The four reactions represent color tests made on the urine. Ehrlich's test is a diazo dye reaction; Moriz Weiss' test is made by adding potassium permanganate to the urine, and Petzetaki's test is made by adding aqueous solution of iodine to the urine; de Silvestri's test is also a color reaction, frequently used in the diagnosis of typhoid fever.

These tests have been suggested as of importance in the diagnosis of tuberculosis. Each test was made by Battista in 60 cases of tuberculosis in children. In instances of tuberculous infection in an early stage these tests were practically never positive; in instances of tuberculosis in the later stages, when many clinical symptoms were present, the tests were frequently positive.

Battista concludes that the tests are of no value in the diagnosis of tuberculosis because they are negative when the disease is minimal and because they may be positive in infections other than tuberculosis.

HIGGINS, Boston.

THE GRANULAR VIRUS AND PRIMARY TUBERCULOUS INFECTION. G. FIORE, Riv. di clin. pediat. **35**:961 (Nov.) 1937.

The tubercle bacillus also exists in the form of a granular virus. The granules are visible under very high magnification and are filtrable. The tubercle bacillus has been found to change into the granular virus in the presence of extracts of brain, muscle and lymph gland. Tuberculous infection can thus easily pass through tissue barriers, enter certain organs and there lead to the formation of tubercles. The virus is believed to be the cause of many of the tuberculous manifestations in childhood, especially those in which the lymphatic system is involved.

HIGGINS, Boston.

SUPPURATING BONE SYPHILIS. M. WAISSMANN, Arch. argent. de pediat. **8**:741 (Aug.) 1937.

Waissmann reports this condition in an infant 1½ years old. The proximal metaphysis of the right femur was involved and was completely destroyed. No suppuration took place in other areas of osteochondritis. Pneumococcus was the pyogenic agent found in the focus, associated with syphilitic infection.

SCHLUTZ, Chicago.

THE REACTION OF BESREDKA IN THE TUBERCULOUS CHILD. C. A. URQUIJO and N. F. M. PAGNIEZ, Arch. argent. de pediat. **8**:769 (Aug.) 1937.

The authors compared the results obtained by carrying out the complement fixation test with tuberculous antigen on the cord and the maternal blood simultaneously.

The result was positive in 21 of 31 cases with the maternal blood and in 20 cases with the blood from the umbilical cord of the infant.

In 7 of the 20 cases in which the reaction was positive with both the mother's and the infant's blood, a higher antibody content was found in the maternal blood. In the infant's blood the antibody content was found high in 7 cases and average but not high in 6. The authors are of the opinion that anticomplementary factors may exist in the blood of the newborn.

SCHLUTZ, Chicago.

TECHNIC OF THE VON PIRQUET TEST. O. LOPES COSTA, Arch. de pediat., Rio de Janeiro **10**:77 (Nov.) 1937.

The author, who uses a linear scarification, believes that the reaction should be described as 1, 2, 3 or 4 plus, depending on the amount of induration.

SANFORD, Chicago.

SYPHILITIC PERIOSTITIS OF THE HUMERUS. A. AGUILAR, Arch. de pediat., Rio de Janeiro **10**:85 (Nov.) 1937.

Aguilar reviews the different forms of periostitis. SANFORD, Chicago.

CONTROL OF TUBERCULOSIS IN RIO DE JANEIRO. J. FREIRE DE VASCONCELOS, Arch. de pediat., Rio de Janeiro **10**:123 (Dec.) 1937.

Patients with tuberculosis are cared for in special clinics and designated institutions. They are under the care of a district federal inspector of infant hygiene and a director of maternal and child health. The actual control is from the Division of Maternal and Child Health. SANFORD, Chicago.

DIFFICULTIES IN THE DIAGNOSIS OF TUBERCULOSIS IN CHILDHOOD. R. A. Echevarria, Bol. Soc. cubana de pediat. **9**:333 (Aug.) 1937.

The differential diagnosis is especially difficult in cases in which there is a dystrophic condition. It is particularly difficult to decide whether the pulmonary involvement is of tuberculous origin or due to a minor infection. There are no characteristic clinical symptoms for either condition. Roentgenographic demonstration of enlargement of mediastinal glands is not sufficient evidence. Many minor pulmonary infections can cause such enlargement. Critical evaluation of all clinical data with the roentgenographic findings will help in the differentiation. Sometimes even autopsy will not reveal the presence of tuberculous foci in the gross specimen although their presence is demonstrable in the microscopic section. SCHLUTZ, Chicago.

ATELECTASIS IN PULMONARY TUBERCULOSIS OF CHILDREN. R. W. MÜLLER, Monatschr. f. Kinderh. **71**:1 (Aug.) 1937.

Müller gives eight roentgenograms illustrating pulmonary involvement in children. Most of the conditions shown cannot be diagnosed clinically, including scattered lesions of phthisis, perifocal infiltrates and early infiltrates. He reviews the literature and discusses the pros and cons of Rösle's theory that all these lesions start primarily with small foci of atelectasis. GERSTLEY, Chicago.

THE BCG VACCINE. K. E. BIRKHAUG, Nord. med. tidskr. **14**:1333 (Aug. 4) 1937.

This is a critical analysis of experimental and clinical data. BCG vaccine is relatively avirulent, but BCG bacilli cannot be regarded as a virus fixé. The vaccine is harmless for man and animals. The allergizing and immunizing properties are best elicited by intradermal injection of the vaccine. The oral method of administration should be abandoned. It is not possible to determine with scientific accuracy the degree of the increase in specific resistance acquired through vaccination. Some rational clinical studies suggest that BCG intradermally injected is capable of reducing morbidity from tuberculosis among infants and adults exposed to tuberculous infection. Other beneficial factors besides specific immunity may, however, play a role in this result. There is no reason to abandon the nonspecific public health measures used hitherto. The vaccine should be reserved for persons whose reaction to tuberculin is negative and who run the risk of being infected with tuberculosis in the immediate future.

WALLGREN, Göteborg, Sweden.

TERTIARY SYPHILITIC LESIONS OF BONES IN AN INFANT. G. FORSMAN, Nord. med. tidskr. **14**:1724 (Oct. 16) 1937.

The mother had syphilis, which had been insufficiently treated and was altogether neglected during her pregnancy. The child, whose weight at birth was 3,220 Gm., did not show any symptoms of syphilis. The mother did not mention her previous syphilitic infection. When the child was 1 month old,

a swelling of the right leg was observed. The roentgen examination showed multiple exuberant periostitic processes of the long bones and, besides, a large gummatous defect in the right femur and another in the right humerus. The Wassermann test was positive in both mother and child. The latter had sanguinolent rhinitis, but the spleen and liver were not enlarged. After antisyphilitic treatment, a rather rapid recovery set in, with disappearance of the lesions in the bones.

WALLGREN, Göteborg, Sweden.

TUBERCULIN ANERGY IN A CASE OF BONE TUBERCULOSIS. S. LINDGREN, Svenska läk.-tidning. **34**:1379 (Oct. 1) 1937.

A boy of 3 was treated at the Academic Hospital of Uppsala, Sweden, for spina ventosa that was clinically, roentgenologically and histologically (biopsy) typical, but he did not react to large doses (from 10 to 100 mg.) of tuberculin. Tubercle bacilli were not demonstrated.

WALLGREN, Göteborg, Sweden.

TUBERCULIN TESTS IN SCHOOL CHILDREN. A. HELMER, Svenska läk.-tidning. **34**:1612 (Nov. 19) 1937.

Patch tests were made on 370 school children 7 years of age, and those who reacted negatively were tested intracutaneously with 0.1 mg. of tuberculin; 38.4 per cent of the children reacted to the former test and, in addition, 11.1 per cent reacted to the latter test. Thus 49.5 per cent of the children were infected. Only 4.1 per cent of them had roentgenologic signs and an increase in sedimentation rate, and of these children only 3 (1.6 per cent of all who were tested) had tuberculous lesions that seemed to be active. No child had to be sent to a hospital or to leave school.

WALLGREN, Göteborg, Sweden.

Diseases of Blood, Heart and Blood Vessels and Spleen

THE USE OF FERROUS GLUCONATE IN THE TREATMENT OF HYPOCHROMIC ANEMIA. P. REZNIKOFF and W. F. GOEBEL, J. Clin. Investigation **16**:547 (July) 1937.

Ferrous gluconate, prepared in the absence of oxygen, was used in the treatment of 13 patients suffering from hypochromic anemia. Four patients who showed toxic reactions to other iron compounds were able to take ferrous gluconate without any undue distress. This preparation, compared with other iron preparations, resulted in utilization of a higher percentage of the iron, more satisfactory reticulocyte responses and rapid daily increases of hemoglobin.

GUEST, Cincinnati.

STUDIES OF THE PRINCIPLE IN LIVER EFFECTIVE IN PERNICIOUS ANEMIA: IV. THE THERAPEUTIC ACTIVITY OF ITS MULTIPLE FACTORS. B. M. JACOBSON and Y. SUBBAROW, J. Clin. Investigation **16**:573 (July) 1937.

Studies of the therapeutic activity of purified liver extract in pernicious anemia suggest that the hemopoietic effect may be exerted by an augmentative action of at least three chemically distinct accessory factors on the activity of a primary factor. Of the three known accessory factors, one is l'tyrosine, another contains a complex purine, and the third is a peptide.

GUEST, Cincinnati.

RECENT ADVANCES IN THE BLOOD COAGULATION PROBLEM. H. EAGLE, Medicine **16**:95 (May) 1937.

Eagle analyzes experimental studies of his own and of other authors and concludes that coagulation of the blood probably involves two reactions:

1. Prothrombin + calcium + platelets → thrombin
2. Thrombin + fibrinogen → fibrin

Trypsin and certain proteolytic snake venoms can replace calcium and platelets in activating prothrombin to thrombin; this and other evidence suggests that calcium and platelets together constitute a protelolytic enzyme, analogous to trypsin. Recent studies confirm the original concept of Schmidt that thrombin likewise is a proteolytic enzyme which splits fibrinogen to form fibrin. Papain and certain snake venoms, all proteolytic substances, convert fibrinogen to a gel resembling fibrin.

The cause of the failure of circulating blood to clot is unknown. It may be that shedding of blood activates the platelets through oxidation, loss of contact with a foreign substance or some unknown process.

The cause of the delay in coagulation in hemophilia is unknown. The prothrombin of the hemophiliac is only slowly activated to thrombin. Eagle found that addition of normal or hemophilic platelets in sufficient quantity accelerated the formation of thrombin to a normal level. Snake venoms have recently been used to arrest bleeding from skin and mucous membranes. Eagle discards the hormone theory as to the cause of hemophilia.

No satisfactory explanation has yet been offered for the hemorrhages in thrombocytopenic purpura. The number of platelets present is sufficient to cause in vitro coagulation almost within normal limits. Delayed retraction of the clot is perhaps a factor.

Recent works suggest that the bleeding tendency in jaundice may be due to a deficiency in prothrombin. It is fairly certain that the noncoagulability of blood in animals after anaphylactic shock is due to a marked increase in antithrombin in the plasma. It is doubtful whether there is a causal relationship between the fibrinogen content of the plasma and the sedimentation rate of the erythrocytes.

Recent experiments suggest that thrombi are simply in vivo blood clots initiated by the agglutination of platelets at foci of irritation along the wall of the blood vessel.

LIMPER, Louisville, Ky.

HEREDITARY OVALOCYTOSIS (HUMAN ELLIPTICAL ERYTHROCYTES): OBSERVATIONS ON TEN CASES IN ONE FAMILY. M. B. STRAUSS and G. A. DALAND, New England J. Med. **217**:100 (July 15) 1937.

The hereditary nature of ovalocytosis was suspected by Dresbach and was established by Hunter and Adams.

The inheritance and morphologic aspects as observed in a study of every member of a family of 36 persons, 10 of whom had this trait, are recorded in this paper, together with certain observations on the physiology of oval erythrocytes. The changes observed at necropsy in one of these persons, who had oval erythrocytes and who died of an unrelated condition, are also given.

The conclusions are:

1. Ovalocytosis is a condition of human erythrocytes that is characterized by an abnormality of cell shape, which is inherited as a mendelian dominant unit character.

2. The peculiarity is inherent in the erythrocytes and is not affected by washing the cells in salt solution, by resuspending them in normal plasma or by incubation.

3. The resistance of oval erythrocytes to hypotonic salt solution does not differ from that of normal erythrocytes.

4. The condition produces no symptoms or disability of any kind.

5. Ovalocytosis is entirely distinct from and has no features in common with sickle cell anemia or the sickle cell trait.

6. The oval shape of the erythrocyte is assumed after the extrusion of the nucleus and is developed fully only after the disappearance of the reticulum.

GENGENBACH, Denver.

FACTORS INFLUENCING SEDIMENTATION RATE OF ERYTHROCYTES. JOSE ZOZAYA, Proc. Soc. Exper. Biol. & Med. **36**:182 (March) 1937.

Zozaya found that there was a logarithmic relation between the sedimentation rate of the erythrocytes and the number of red blood cells. The euglobulin fraction of the serum proteins had a slightly greater accelerating effect than the fibrinogen. The albumin fractions accelerated the sedimentation rate. There was no statistical difference of changes in the albumin-globulin ratio and in the level of the total proteins affecting the sedimentation rate. Magnesium and calcium had a greater inhibiting effect than potassium and sodium. Lecithin produced a marked retardation in the rate, while cholesterol, to a less extent, exerted an accelerating influence. Under the ultramicroscope, lecithin caused a dispersion of red cells, the shape becoming more spherical, while cholesterol increased the closeness of the rouleaux. There were individual differences in the same plasma produced by erythrocytes from various sources. The sedimentation rate of ox corpuscles is slower than that of horse or human cells in the various (ox, human and horse) plasmas. The sedimentation rate of human cells is faster in the different plasmas, especially in ox plasma. These are intrinsic factors in the plasma and in the erythrocytes that affect the velocity of sedimentation which cannot be predicted, making the sedimentation test theoretically difficult to evaluate.

HANSEN, Minneapolis.

COBALT CONTENT OF IRON COMPOUNDS AND ITS POSSIBLE RELATION TO TREATMENT OF ANEMIA. E. J. UNDERWOOD, Proc. Soc. Exper. Biol. & Med. **36**:296 (April) 1937.

Analyses of several common laboratory compounds of iron reveal significant though variable quantities of cobalt. The administration of cobalt recently brought about cure of certain diseases in various animals, such as sheep and cattle, which had been benefited by large doses of iron compounds, thus proving that the beneficial effect of the iron compounds was due to cobalt, which is present as an impurity. It has been suggested that a similar improvement may be obtained in human beings with anemia by the administration of cobalt. This study was undertaken to determine the content of this element in the various iron compounds commonly used therapeutically as a basis for further study on human subjects, especially in regard to those conditions in which massive doses are employed.

HANSEN, Minneapolis.

A CASE OF GOAT'S MILK ANEMIA. P. MÖDLINGER, Orvosi hetil. **81**:247 (March 13) 1937.

A 13 month old infant, a boy, was admitted to the White-Cross Hospital in Budapest because of undernutrition and poor appetite. He had been normal at birth, had been nursed two months and later received mother's milk and goat's milk in the dilution 1:2. From 5 months of age he was fed only with goat's milk. The rice was cooked with goat's milk also. He received only small amounts of broth and vegetables, which he did not like and most of which he vomited. The skin was pale, and there were many petechiae. The red blood cell count was 960,000; the hemoglobin content, 30 per cent; the color index, 1.5. In the beginning, the goat's milk anemia was treated only by substituting cow's for goat's milk, but the boy showed no improvement in two weeks. Then blood transfusions (350 cc.) and injections of an extract of liver were given. Rapid recovery followed. This is the first case of goat's milk anemia to be described in Hungary.

GÖTTCHE, Budapest, Hungary.

HEMOPHILIA WITH LIFE-MENACING SUBCUTANEOUS BLEEDING. B. ROOS, Hygiea **99**:385 (May 31) 1937.

A boy of 11 years had had a tendency to bleed after trauma, extraction of teeth and other lesions since his first year. Both parents were deaf-mutes. There

was no heredity suggesting a hemorrhagic diathesis. He was admitted to the hospital because of hematuria. The bleeding time was two and five-tenths minutes; the clotting time, forty-five minutes. After a slight trauma against the spine a large subcutaneous hematoma appeared on the back. The hemoglobin level decreased from 90 to 25 per cent in two days. Blood transfusion was performed, and the bleeding stopped. A week later the hemoglobin was 60, and after another three weeks the hematoma had disappeared. The thrombocyte count was 296,000. The blood calcium content was 8.2 mg. per hundred cubic centimeters. The clotting time was seventy-two minutes.

WALLGREN, Göteborg, Sweden.

SUBACUTE LEUKEMIA WITH JOINT SYMPTOMS AND REMISSION. D. JEPPSON, Svenska läk.-tidning. **34**:642 (April 30) 1937.

A boy of 5 years was first examined Jan. 5, 1936, because of pains in the joints. He had swelling of the right index finger, pains but no objective pathologic involvement of the arms and legs, great enlargement of the spleen and liver, excessively rapid sedimentation of the red blood cells, fever and hypochromic anemia. The white blood cell count was 5,000, with 70 per cent mononuclears. Roentgenologic examination of the swelling of the right index finger showed localized decalcification. The pains in the joints and the fever continued, and the blood picture changed into one more typical of leukemia, while the anemia increased. After a short period of remission, with a remarkably rapid improvement in the blood picture and in the general condition of the boy, he eventually grew worse and died April 13. At the postmortem examination a leukemic infiltration of the right index finger was demonstrated.

WALLGREN, Göteborg, Sweden.

ACUTE LYMPHATIC LEUKEMIA WITH SKELETAL DEVIATIONS. J. MUNK and J. H. NAUTA, Maandschr. v. kindergeneesk. **6**:407 (July) 1937.

Munk and Nauta describe acute lymphatic leukemia in a boy of 11 years, accompanied by extensive changes in the skeleton and also at places where no swelling or tenderness was present. A patient with acute myeloid leukemia showed, on closer examination, analogous skeletal deviations. The importance of looking for these skeletal changes in cases of leukemia in childhood is stressed.

VAN CREVELD, Amsterdam, Netherlands.

PURPURA HAEMORRHAGICA AFTER THE USE OF SEDORMID. P. H. KRAMER, Nederl. tijdschr. v. geneesk. **81**:3345 (July 10) 1937.

In connection with the report of 2 cases of acute thrombopenic purpura (Werlhof's disease) following the use of the hypnotic sedormid (allylisopropylacetylcarbamide), reports of similar cases are quoted from the literature and the importance of knowledge of the picture of sedormid purpura is stressed. Kramer is convinced that withdrawal of the drug is such cases is sufficient to effect a complete recovery.

VAN CREVELD, Amsterdam, Netherlands.

THROMBOPENIA WITH PURPURA (WERLHOF'S DISEASE) FOLLOWING THE USE OF SEDORMID. P. VAN ANDEL and J. GROEN, Nederl. tijdschr. v. geneesk. **81**:3348 (July 10) 1937.

This is an extensive description of 3 cases of thrombocytopenic purpura in adults due to the use of sedormid (allylisopropylacetylcarbamide), with spontaneous recovery after the drug had been omitted and reappearance of the symptoms when it was taken again.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of Lungs, Pleura and Mediastinum

RENAL PHYSIOLOGY IN LOBAR PNEUMONIA. L. E. FARR and T. J. ABERNATHY, J. Clin. Investigation **16**:421 (May) 1937.

Renal physiologic studies were made on 28 patients with lobar pneumonia, observed over varying periods of time up to six months. Determinations were made of the urea clearance every three days until the crisis and at variable intervals thereafter. Other data reported concerned the urea nitrogen in the blood, the urinary volume, sediment, protein and p_H and the types of pneumococci found in these patients.

The urea clearance during the disease showed a sharp difference between the older and the younger patients, which was interpreted as due to a decrease of renal resilience with increasing age. The patients under 40 years of age showed marked elevation of the urea clearance, persisting about one month and independent of the type of pneumonia or of therapy. The older age group showed little change in the urea clearance. Observation of the urinary sediment in all groups showed a strong tendency for all abnormal elements to disappear with the establishment of an adequate fluid balance. No significant changes in blood pressure were associated with the changes in urea clearance.

GUEST, Cincinnati.

POSTOPERATIVE ATELECTASIS: REPORT OF A CASE, PROMPTLY RELIEVED BY SIMPLE MEASURES. L. SAUER, J. Pediat. **11**:321 (Sept.) 1937.

In a 5 year old boy, on the morning following an appendectomy, atelectasis of the right lung developed. He was rolled on the unaffected side, steam inhalations were given, the foot of his bed was elevated, oxygen and carbon dioxide were administered intermittently by gas machine, all without any change in his condition. In the region of greatest dulness, just below and median to the right scapular angle, a clenched fist was firmly pressed and several short forceful blows with the flat right palm were directed against the fist. This was repeated several times during the next hour. For two hours a profuse amount of mucus was discharged from the nose and mouth; then a gelatinous hemorrhagic inspissated plug of mucus was coughed up and expectorated. Following this the atelectatic middle and lower lobes were reinflated and all symptoms disappeared, with complete recovery.

RAUH, Cincinnati.

THE DIAGNOSIS OF NONOPAQUE FOREIGN BODY IN THE TRACHEOBRONCHIAL TREE, WITH A DESCRIPTION OF THE PHYSICAL AND X-RAY FINDINGS. M. F. ARBUCKLE, J. Pediat. **11**:356 (Sept.) 1937.

The diagnosis of a nonopaque foreign body in the tracheobronchial tree may be difficult. The history must be taken carefully. The physical signs will be: unilateral or bilateral obstructive emphysema, shifting obstructive emphysema, atelectasis, or a combination of obstructive emphysema and unilateral atelectasis. Certain pathognomonic signs are described. A nonimpacted foreign body may be thrown by the cough impulse upward to where it strikes the lower surface of the vocal cords. With the mouth open, the impact may be heard and is known as the audible slap. The same impulse may be felt by placing the fingers against the walls of the larynx; it is then known as the palpatory thud. If the air current is partially blocked by a foreign body in the tracheobronchial lumen, a wheezing breath sound is heard, more marked on exhalation; it is best heard by placing the ear or stethoscope before the open mouth. This sign is known as the asthmatoid wheeze. Arbuckle has observed another sign, a characteristic "split cough," which has in general the characteristics of the asthmatoid wheeze. Fluoroscopic examination is of value in these cases for comparison of the movements of the walls of the chest and of the diaphragm on the two sides and any changes of position of the heart during the respiratory cycle. Roentgenograms made in pairs, one at the end of full inspiration and one at the end

of full expiration, are of great value in demonstrating unilateral or bilateral obstructive emphysema, atelectasis, the position of the heart and the shift of the heart. When there is a doubt as to the presence of a foreign body, bronchoscopic examination should be carried out. Arbuckle presents case reports, with roentgenograms, illustrating the diagnostic features emphasized.

RAUH, Cincinnati.

BRONCHIAL ASTHMA AS A PEDIATRIC PROBLEM. W. C. SPAIN, M. Rec. **146**:112 (Aug. 4) 1937.

Spain found in a study of 462 cases of bronchial asthma that the stronger the factor of inheritance the greater was the incidence and the earlier the age of the onset of clinical symptoms. He divides his patients into the "skin positive group" and the "skin negative group." He thinks that the most important exciting causes are foods and inhalants, such as pollens, dust, toilet powders, the epithelial scales of feathers or of animal hairs and the lint of cotton, silk or wool. He points out the importance of early treatment and discusses fully the general management and treatment of the asthmatic patient. He gives the results of treatment in his patients.

WILLIAMSON, New Orleans.

TREATMENT OF EMPYEMA. T. J. KINSELLA, Minnesota Med. **20**:502 (Aug.) 1937.

In an excellent article Kinsella discusses the principles of treatment, the types of treatment and the criteria for the choice of the various methods. He concludes that there are no definite rules for the treatment of this condition and that each patient must be considered individually and the method or methods best suited to his particular problems chosen for use. He also advocates the simplest type of treatment adequate for the occasion. Complicated methods may give good results with special equipment but require much more attention and have little place in general work.

ANDERSON, Minneapolis.

RELATION OF UPPER RESPIRATORY TRACT INFECTION TO EARLY BRONCHIECTASIS IN CHILDREN. J. H. EBBS, Proc. Roy. Soc. Med. **30**:1407 (Sept.) 1937.

Ebbs made his observations on 200 children with pneumonia and related conditions who came to autopsy; 85 had infected sinuses, 133 had infected ears and 160 had both infected sinuses and infected ears. Having found such a high incidence of sinusitis and otitis media, Ebbs decided to look further into the actual pathologic conditions in the lungs. He was surprised in a number of cases to find bronchiectasis. The best study and summary of the pathologic changes characteristic of bronchiectasis which he had encountered was that by Erb, published in 1933. In the article by Ebbs are shown all the changes which must occur in the lung from the time that the earliest inflammatory lesions in the bronchi occur until chronic bronchiectasis is well established. Then follow in the article several reproductions of photomicrographs of sections of lung showing the sequence of histologic changes, varying in degree from acute bronchitis up to advanced bronchiectasis. Where one ends and the other begins in childhood is impossible to say, since chronic bronchitis gradually and insidiously merges into bronchiectasis. Each illustration is accompanied by a brief history.

In conclusion Ebbs makes two general statements about treatment: 1. When the chronic stage of the disease is reached, the only hope of complete recovery is in the removal or destruction of the diseased area. 2. A change of habitat to the country or to the sea is beneficial. The vast majority of cases occur in the poorer classes, and so there is need of hospitals or convalescent homes where one may send city children suffering from chronic bronchitis or convalescent from pneumonia.

WILLIAMSON, New Orleans.

ABSCESS OF THE LUNG. T. SCHRIRE, South African M. J. **11**:812 (Nov. 27) 1937.

It is almost impossible, states Schrire, for an abscess of the lung to form unless bronchial obstruction to a lesser or greater degree is present. The earliest phenomenon following such an obstruction is atelectasis. In childhood the three primary causes of formation of abscess of the lung are: operation, a foreign body and pneumonia. In the adult an underlying obstructing carcinoma of the bronchus must always be considered. The usual symptoms are cough, production of sputum, pyrexia and clubbing of the fingers (this appears after six or eight weeks and disappears after cure). The diagnosis of an abscess of the lung can never be made with assurance on physical examination alone; subsidiary examinations (roentgen and bronchoscopic) are always essential if the diagnosis is to be certain. Treatment consists of medical, bronchoscopic and surgical measures. A detailed description of the technic of surgical treatment is given.

GONCE, Madison, Wis.

SHOULD THE TREATMENT OF PURULENT PLEURITIS IN CHILDREN BE MEDICAL OR SURGICAL? M. ACQUA, Méd. inf. **8**:309 (Oct.) 1937.

An analysis was made of the observations made on children treated for empyema in the surgical and pediatric clinics of the University of Messina. The highest mortality was in those in the first and second years of life.

Before a definite decision as to the method of treatment can be made, each patient must be studied as to age, general condition, temperature curve, physical findings and bacterial flora of the exudate. In general, pneumococcic pleuritis occurring during the first two years of life responds better to medical management, but surgical intervention should be resorted to if four or five aspirations do not result in improvement. In older children, as a rule, surgical treatment gives the better results.

HIGGINS, Boston.

VACCINE THERAPY IN BRONCHOPNEUMONIA OF CHILDREN. M. RADICI and G. BRESSA, Lattante **8**:503 (Sept.) 1937.

Observations were made on 283 children with bronchopneumonia, 137 of whom were treated symptomatically and 146 of whom received, in addition to symptomatic treatment, injections of a mixed vaccine consisting of an emulsion, in physiologic solution of sodium chloride, of influenza bacilli, pneumococci, streptococci and micrococci (M. catarrhalis). There was definite diminution in the mortality of infants under 1 year who received the vaccine. There was slight diminution in the death rates of children in the second and third year of life, but among children over 3 years of age the mortality statistics were much better for those not receiving the vaccine. Altogether, the statistics show a mortality of 14 per cent among nonvaccinated and of 11 per cent among the vaccinated infants. The children receiving the vaccine tended to be sick a shorter time—fourteen days as contrasted with twenty-three days. Complications occurred in 16 per cent of the vaccinated and 19 per cent of the nonvaccinated children. The authors feel that their results indicate that the vaccine therapy was beneficial.

HIGGINS, Boston.

COMBINATION OF A MUSCULAR AND AN INFLAMMATORY MARGINAL SHADOW IN THE REGION OF THE PLEURA. BENNHOLDT-THOMSEN and H. H. KALBFLEISCH, Ztschr. f. Kinderh. **59**:45 (Aug. 2) 1937.

A case of spontaneous pneumothorax enabled the authors to substantiate the Bennholdt-Thomsen contention (*Ztschr. f. Kinderh.* **58**:523, 1936) that marginal shadows in the region of the pleura may be normal or pathologic. Roentgen examination before and after removal of a pleura which was the seat of a fibrinopurulent exudate proved that a marginal shadow which was observed was

produced mainly by the musculature of the thoracic wall. As an incidental finding, a shadow in connection with ribs (caused by subpleural fat) is mentioned. The article is illustrated by roentgenograms.

SIEMSEN, Chicago.

CLASSIFICATION OF PNEUMONIAS IN CHILDREN. R. STANKIEWICZ, Pedjatrja polska **17**:1 (Jan.-Feb.) 1937.

Stankiewicz discusses extensively the classification of pneumonias. Since Hippocrates' time there have been attempts to classify pneumonias from the pathologic standpoint, from observations made at postmortem examinations, from roentgenologic findings, on the basis of causes, from the point of view of symptoms and from clinical observations. None of the attempts has brought about complete classification of pneumonias. The author comes to the conclusion that it is a difficult problem to classify pneumonias satisfactorily.

KRUPINSKI, Chicago.

HAEMOPHILUS INFLUENZAE (TYPE B) AS A CAUSE OF AN INFECTION OF THE RESPIRATORY ORGANS. J. VAN LOOKEREN CAMPAGNE, Maandschr. v. kindergeneesk. **7**:43 (Nov.) 1937.

A boy of 2 years showed an illness which began as phlegmonic laryngitis. A month later, the left lung yielded pus in which the bacillus of Pfeiffer, type b, was identified. The author stresses the fact that different types of the bacillus of influenza can be differentiated by precipitation and agglutination.

VAN CREVELD, Amsterdam, Netherlands.

THE PHYSIOLOGY OF THE BRONCHIAL TREE. E. HUIZINGA, Nederl. tijdschr. v. geneesk. **81**:3829 (Aug. 27) 1937.

A number of physiologic problems in connection with bronchographic examination are considered. The trachea and peripheral airways may show extensive movement though at the site of the bifurcation little displacement is seen. The bronchi spread out during inspiration; the angle between them may also become narrower on intense diaphragmatic respiration. With deep respiration the diameter shows great variation, even in adults. In the smaller bronchi the variation is such (the diameter increasing twofold or threefold on inspiration) that its explanation becomes difficult. The variation in the lumen is also present when the effect of change in pressure can be ruled out; the lumen varies with the volume of the lung. This must have an important bearing on expectoration. Bronchial peristalsis could not be observed. It is shown that the respiratory changes may produce pictures which might easily give rise to a wrong explanation.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of the Gastrointestinal Tract, Liver and Peritoneum

DIAGNOSIS OF THE CAUSES OF LOW-GRADE ABDOMINAL PAIN IN CHILDREN. J. E. BRADLEY, M. Clin. North America **21**:1373 (Sept.) 1937.

Several cases are discussed in which the cause of abdominal pain was obscure but in which the pain proved on careful study to result from such varied conditions as lead poisoning, tuberculous mediastinal glands, peritoneal bands and allergy. In many of these cases the problem will require for its solution every diagnostic resource available, and none should be neglected. While in the great majority of the cases the cause of such low grade abdominal pain is comparatively trivial, a correct diagnosis only should satisfy the careful clinician.

EUGENE H. SMITH, Ogden, Utah.

ACUTE APPENDICITIS IN INFANTS, CHILDREN AND ADULTS. G. I. MILLER, M. Rec. **146**:121 (Aug. 4) 1937.

The paper may be summarized as follows: A sudden onset of abdominal cramps in children or adults suggests appendicitis unless a definite cause for the attack can be diagnosed.

Babies 2 days old and older are able to withstand operations.

Preoperative diagnosis of a mobile cecum may save an operation for appendicitis. A mobile cecum with its appendix is located higher in the presence of a gravid, enlarged uterus or a tumor growing from the pelvis. A preoperative diagnosis of mobile cecum is easily and definitely made by inspection of the abdomen.

When peritonitis due to a perforated appendix is diagnosed, the maintenance of Fowler's position preoperatively for a short period will localize the infection to the pelvic area.

An infected peritoneal cavity is to be drained.

The use of autogenous vaccine, injections of prontosil (a derivative of sulfanilamide), injections of dextrose in saline solution, blood transfusions, administration of stimulants and gastric lavage may save a life.

WILLIAMSON, New Orleans.

CONGENITAL HYPERTROPHIC PYLORIC STENOSIS. O. W. ROWE, Minnesota Med. **20**:508 (Aug.) 1937.

Rowe presents a conclusion obtained from a study of 50 consecutive cases of congenital hypertrophic pyloric stenosis without a death. The importance of early diagnosis, before severe nutritional disturbances have taken place, is emphasized. When the stenosis is mild and medical treatment is employed, the value of breast milk or evaporated milk thickened with cereal is emphasized. Rowe feels that atropine, if used, should be used most cautiously, as he considers it a dangerous drug. In practice he finds phenobarbital as effective and much safer. He advocates surgical treatment for this condition except when it is extremely mild. The necessity for prolonged hospitalization and the danger of intercurrent infection plus the expense make medical treatment inadvisable in most instances. He feels that surgical treatment with proper postoperative care is quick, sure and permanent in its results. The Fredet-Rammstedt submucous pyloroplasty was the operation used in his series. Advice as to the care of the patient prior to and after operation is given clearly and in a manner to render the directions usable.

ANDERSON, Minneapolis.

SODIUM CHLORIDE CONTENT OF GASTRO-INTESTINAL SECRETIONS. V. S. DICK, W. G. MADDOCK and F. A. COLLER, Proc. Soc. Exper. Biol. & Med. **37**:318 (Nov.) 1937.

Study of the sodium and chlorine contents of various gastrointestinal secretions and vomitus and of discharges in biliary and intestinal fistulas indicates that the amount of these elements lost is slightly less than that in a similar volume of Ringer's solution. The authors believe that a reliable rule for the replacement of sodium chloride lost in gastrointestinal secretions is to administer Ringer's solution parenterally volume for volume for the gastrointestinal secretion lost.

HANSEN, Minneapolis.

POWDERED APPLE IN DIARRHEA. H. BARIL, Union méd. du Canada **66**:841 (Aug.) 1937.

Baril has been using apple powder in all cases of diarrhea occurring on his service. Of 37 infants under 10 months of age whom he treated, 27 recovered within forty-eight hours. Of the infants in whom the treatment was unsuccessful,

5 were premature, 1 had bronchopneumonia with diarrhea and 1 had pneumococcic meningitis. Baril feels that the pectin is the therapeutic factor.

DAFFINEE, Boston.

TWO CASES OF PYLORIC STENOSIS TREATED WITH EUMYDRINE. R. H. DOBBS, Proc. Roy. Soc. Med. **30**:1193 (Aug.) 1937.

The first patient was admitted to the hospital when 3 weeks old with all the symptoms of pyloric stenosis. On the fifth day after admission roentgenograms showed a barium sulfate meal to be entirely retained in the stomach up to six hours. The following day treatment with atropine methylnitrate was commenced. The first two days 25 minims (1.5 cc.) of a 1:10,000 solution were given twenty minutes before each feeding. Subsequently the dose was reduced to 15 minims (0.9 cc.) at each dose. With this treatment vomiting ceased entirely on the fifth day. On the twenty-third day after admission the use of the drug was discontinued for four days. The vomiting returned on the second day and ceased the day after the administration of this drug was resumed. Roentgenograms taken on the twenty-eighth day showed that there was still some retention but that a great deal of the barium sulfate had passed into the duodenum in four and a half hours. The dose was gradually reduced until at the end of twelve weeks its use was stopped entirely, and the vomiting did not return. Before beginning treatment with atropine methylnitrate, sufficient fluids in the form of salt solutions should be administered in order to replace the fluid and chlorides lost. Efficient replacement of both water and chlorides is essential before the administration of this drug is begun if toxic symptoms are to be avoided. A second case is reported in an infant 5 weeks old.

WILLIAMSON, New Orleans.

CONGENITAL PYLORIC STENOSIS. B. SANCHEZ SANTIAGO, R. PEREIRAS and F. SALA, Arch. de med. inf. **6**:430 (Oct.-Dec.) 1937.

The case histories of 7 infants with congenital pyloric stenosis are given, with roentgenograms. The authors believe that each case should be given serial roentgenographic or fluoroscopic observations for eight hours after ingestion of a barium sulfate meal.

SANFORD, Chicago.

NYCTURIA IN DISEASES OF THE LIVER AND IN PERNICIOUS ANEMIA. O. JERVELL, Acta med. Scandinav. **93**:359, 1937.

In normal persons the urinary output during the night is less than two thirds of that during the day. Forsgen has shown that liver function has an assimilatory phase during the night and a secretory phase during the day; the former is connected with water retention, owing to storing of glycogen, and therefore less urine is formed. Nycturia is a sign of disturbance in the rhythmic function of the liver.

Sixty patients were studied. During the night no food or fluid was taken. Twenty-four of 26 who had hepatic disease and 15 of 18 who had pernicious anemia, but only 1 of 6 who had secondary anemia, had nycturia. The chloride, nitrogen and urobilin excreted grossly paralleled the diuresis.

KAJDI, Baltimore.

TWO CASES OF RETROPERITONEAL CYSTIC TUMOR IN CHILDREN. N. FROSTE, Hygiea **99**:844 (Nov. 30) 1937.

Two girls, 6 and 7 years of age, who for some time had had pains in their abdomens were operated on under the erroneous diagnosis of appendicitis. In both cases a cystic retroperitoneal benign tumor was extirpated. Recovery followed. The source and nature of the tumors are unknown.

WALLGREN, Göteborg, Sweden.

A Case of Pyloric Stenosis with Relapse. N. Malmberg, Nord. med. tidskr. **14**:1883 (Nov. 13) 1937.

An 8 week old infant had had symptoms of congenital pyloric stenosis since the age of 2 weeks. The vomiting disappeared rapidly with dietetic treatment and administration of atropine. After a symptom-free interval of ten days, the vomiting reappeared. As the treatment previously used did not at this time have any effect, after five and one-half weeks the infant was operated on, with good result.

Wallgren, Göteborg, Sweden.

Treatment of Megacolon Congenitum. J. van Lookeren Campagne, Maandschr. v. kindergeneesk. **7**:9 (Oct.) 1937.

The author is of the opinion that operative treatment of congenital megacolon should be considered only after the classic therapy and dilation of the sphincter ani fail to give satisfactory results. He illustrates this principle by citing two cases.

van Crevald, Amsterdam, Netherlands.

Nervous Diseases

Otitic Meningitis: Report of a Case in Which Treatment Was Followed by Recovery. DeG. Woodman, Arch. Otolaryng. **26**:310 (Sept.) 1937.

A 6 year old boy with otitic meningitis was treated by surgical drainage of the mastoid, frequent transfusions of blood, intravenous and intraspinal injections of convalescent scarlet fever serum, intramuscular injections of a derivative of sulfanilamide (prontosil) and administration of sulfanilamide by mouth. The spinal fluid yielded a growth of streptococcus haemolyticus. The sulfanilamide treatments caused marked cyanosis, which disappeared promptly when these treatments were discontinued. Woodman can only speculate as to why this child made a complete recovery.

Greenwood, Chicago.

Periodic Paralysis. J. B. Gillespie, Arch. Pediat. **54**:569 (Oct.) 1937.

In most cases of periodic paralysis there is a history of incidence in members of the family through several generations. Isolated occurrence of the condition is not common. It is transmitted by both males and females, and at times it may skip a generation. Migraine headaches in certain members may be the equivalent of the paralytic attacks in other members of the same family.

The average age of onset is at puberty. Males and females are equally afflicted. Paralysis is the primary feature in all cases, and in typical form it may involve all the voluntary muscles except those of the face, eyes, tongue, organs of speech, deglutition and sphincters of the rectum and bladder. Improvement in the paralysis may require several hours or even a day. Attacks occur mostly at night. There are no psychic symptoms during an attack, and death seldom occurs from an attack.

The author reports a case of periodic paralysis occurring in a 5 year old boy. There is no history of similar attacks in the immediate or past generations. The seizures began at the age of 18 months, have always been diurnal and have increased in frequency until they now occur several times a day. The paralysis is localized to the lower extremities. Physical examination yields essentially negative results except for the neurologic findings. The deep reflexes, the biceps reflex, the achilles tendon reflex and the knee jerk reflex were absent. All the laboratory data submitted were normal.

The patient has responded satisfactorily to treatment with phenobarbital and bromides, and, for the first time since the onset, has gone several weeks without having any seizures.

Orr, Buffalo.

ALKALIGINES BOOKERI MENINGITIS: REVIEW OF LITERATURE ON GRAM-NEGATIVE BACILLUS MENINGITIS. G. W. KUTSCHER JR., Arch. Pediat. **54**:610 (Oct.) 1937.

Kutscher reports what he considers to be the first case of meningitis due to Bacillus bookeri. The disease occurred in an infant, a girl 4½ months old. She made a complete recovery.

ORR, Buffalo.

TESTS OF VIRUSES OF CHORIOMENINGITIS AND ENCEPHALITIS (ST. LOUIS) WITH SERUM FROM NONPARALYTIC POLIOMYELITIS (NEW YORK CITY, 1935). M. BRODIE, J. Infect. Dis. **61**:139 (Sept.-Oct.) 1937.

Convalescent serum from 24 patients whose illness had been diagnosed as nonparalytic poliomyelitis failed to neutralize the virus of acute aseptic choriomeningitis. Serum from 17 patients, of whom 15 had cerebral manifestations, gave similar negative results with the virus of encephalitis B (St. Louis).

TOOMEY, Cleveland.

HEMOLYTIC STREPTOCOCCUS MENINGITIS: REPORT OF A CASE WITH RECOVERY AFTER THE USE OF SULFANILAMIDE AND ITS DERIVATIVES. J. MILLETT, New England J. Med. **217**:556 (Sept. 30) 1937.

Seven cases of meningitis due to infection by the hemolytic streptococcus in which treatment was by sulfanilamide or its derivatives have been collected from the literature and a case has been added, that of a 13 year old boy. This case is reported in detail. This small series shows 1 death, or a mortality of 12.5 per cent, in contradistinction to a reported mortality of about 97 per cent previous to the use of sulfanilamide and the related products.

GENGENBACH, Denver.

CEREBRAL TUMOURS IN CHILDREN: A PATHOLOGICAL REPORT. R. O. STERN, Arch. Dis. Childhood **12**:291 (Oct.) 1937.

Stern investigated 102 cases of cerebral tumor which occurred in children under the age of 12 years during the period 1921 to 1935. Over one half of these cases occurred in children under 5 years of age. There was no difference in the incidence according to sex. The 62 autopsies in this series of cases formed 2.2 per cent of all postmortem examinations during that period. Fourteen of the cases in which the presence of a tumor was verified at autopsy occurred in children under 2 years of age. Tumors were twice as common below the tentorium as above it. No tumors of the pituitary fossa were encountered, and only 1 in the suprapituitary region. A histologic study was made of 55 of the tumors. Two thirds of these belonged to the glioma group. Well differentiated glioma was as common as the more malignant forms but occurred in situations inaccessible to surgical treatment. There were 6 examples of a malignant glioma, glioblastoma multiforme, a form which, when it occurs, occurs almost invariably in the cerebral hemispheres of adults. In 3 of these cases the growth was found below the tentorium. Four cases of ependymal tumor were included in the series. One of these was in an infant of 5½ months. The more benign gliomas occurred at earlier ages than did those of greater malignancy. Only 1 case of solitary tuberculoma was found.

KELLY, Milwaukee.

SYDENHAM'S CHOREA: ITS COURSE AND RELATIONSHIP TO RHEUMATIC FEVER. S. WILLIAMS, M. J. Australia **2**:590 (Oct. 9) 1937.

A follow-up examination of 66 children who had had the onset of chorea from six months to five years previously showed physical signs of rheumatic heart disease in 19 of them. Of these 19 children, 13 had evidence of heart disease at the onset of the chorea, and 6 evidently acquired the involvement of the heart

subsequently. Forty-one of these children had chorea differing in no way from that in the other 25 except for the absence of cardiac involvement. The number of recurrences of chorea was the same in the two groups; more than half the children had more than one attack. There was no relationship between the number of attacks and cardiac complications. GONCE, Madison, Wis..

PERIPHERAL VASOCONSTRICTOR NEUROSIS: ACROPARESTHESIA (NOTHNAGEL). F. DE FILIPPI, A. BONDUEL and I. FERNANDEZ, Arch. argent. de pediat. **8**:887 (Sept.) 1937.

The authors report this rare condition in a child 12 years old. The physical condition and psyche of the child seemed entirely normal. For some time past it had had both subjective and objective symptoms, confined principally to the extremities and the face. These symptoms consisted of pallor of the face, coldness of the hands and feet, loss of sensation and marbling of the skin. The symptoms were accentuated by cold weather. Reestablishment of the circulation caused relief of these symptoms.

The disorder apparently was purely vasomotor, without any organic lesion of the vessels, and consisted in transitory spasm of the vessels—a condition described first by Nothnagel, who gave it the name "acroparesthesia."

The treatment in this case consisted in the removal of focal infections, the use of quinine hydrochloride and physical therapy. SCHLUTZ, Chicago.

PACCHYMENINGITIS HAEMORRHAGICA OF INFANCY. A. C. GAMBIRASSI and A. N. ACCINELLI, Arch. argent. de pediat. **8**:899 (Sept.) 1937.

After the acute stage has passed, the authors recommend surgical treatment, which consists in the removal of the residual membrane of the involved meningeal area. They have seen no benefit from the subcutaneous injection of gelatin.

SCHLUTZ, Chicago.

SYMPTOMS AND HISTOPATHOLOGIC PICTURE OF GANGLIOCYTOMA OF THE MEDULLA OBLONGATA. E. AMSTAD, Schweiz. Arch. f. Neurol. u. Psychiat. **39**:5, 1937.

Foerster and Gagel classified ganglion cell tumors as gangliocytomas (tumors made up solely of ganglion cells) and ganglioneuromas (tumors which in addition contain nerve fibers). The second group is subdivided into myelinated and amyelinated forms, depending on the presence or absence of myelin sheaths about the new-formed fibers. About 50 cases of ganglion cell tumor of the central nervous system have been reported. Amstad gives the clinical and postmortem observations in a case which he studied.

An underdeveloped youth aged 17 had been subject during childhood to nocturnal choking spells, attacks of dyspnea, nausea, pain in the upper part of the abdomen, difficulty in swallowing and vertigo. During the six months prior to admission to the clinic he lost weight and suffered from weakness, difficulty in swallowing and respiratory embarrassment. Two weeks before death fever, vomiting and persistent hiccup appeared. Extensive aspiration pneumonia, bilateral purulent otitis media and acute swelling of the spleen were observed at autopsy.

Study of the brain revealed internal hydrocephalus and a soft, infiltrating tumor extending from the first cervical segment to the lower limit of the pons, reaching its greatest extent in the right side of the medulla oblongata, at the level of the obex; it projected into the fourth ventricle. Histologically, the tumor was fairly vascular and had a stroma made up of glia cells. In some places septums of hyalinized connective tissue from the thickened pia extended into the tumor. Large vesicular nuclei, each with a definite nuclear membrane and a deeply staining nucleolus, were seen in the tumor. Some cells had two nuclei, but direct evidence

of either mitotic or amitotic division was lacking. The central portion of the cell was pale as a rule, the Nissl granules being confined to the periphery. No definite endofibrils could be demonstrated. Myelin was not seen in the tumor, but otherwise the nerve fibers, which were not regarded as neoplastic, appeared to be intact.

Amstad believes that the tumor developed in earliest childhood. He states that gangliocytoma of the medulla oblongata may produce symptoms at any time between the ages of 10 and 40 but does so most frequently between the ages of 15 and 20. The period elapsing between onset of symptoms and fatal termination varies from six months to ten years; it averages from three to five years. Bulbar involvement is indicated by respiratory and cardiac disturbances, as well as by difficulty in swallowing, vomiting and other gastric symptoms. The degree of involvement of the pyramidal tracts and sensory systems depends on the extent to which the cervical portion of the cord is invaded. Persistent hiccup is an important late symptom.

DANIELS, Denver. [ARCH. NEUROL. & PSYCHIAT.]

TREATMENT OF ACUTE CHOREA WITH BLOCK OF THE SYMPATHETIC NERVOUS SYSTEM. D. M. ZALKAN and E. M. EBICH, Vrach. delo **20**:114, 1937.

Zalkan and Ebich report 15 cases of acute chorea in which treatment consisted of block of the sympathetic trunk with procaine hydrochloride. Therapy was successful in 13 cases; the earlier it was begun the more striking was the result. The effect of block in the early stages was rapid, and in some cases, abortive. Prompt improvement in the symptoms frequently took place on the day following the injection, and all symptoms disappeared in the course of the next four or five days. Decisive improvement was likewise noted in patients with disease of longer duration, but the recovery consumed more time—from ten to fifteen days. These patients were given two or three additional injections. The treatment failed with 2 patients, aged 25 and 15 years, respectively, who had had a long illness—one for one year and one for six months. Good results were obtained in treatment for recurrences as well as in that for disease of recent origin. There were no recurrences in patients who had been cured. The authors experienced no difficulty in applying the method to treatment for children. The procedure consists of injecting into the region of the renal fossa from 60 to 100 cc. of a 0.25 per cent solution of procaine hydrochloride on the side of the predominating symptoms. From one to three injections are given.

EDITOR'S ABSTRACT [J. A. M. A.]

Psychology and Psychiatry

DEFINITION OF "CHILDHOOD" IN PSYCHIATRIC LITERATURE. C. BRADLEY, Am. J. Psychiat. **94**:33 (July) 1937.

There is much confusion as to what constitutes the period of childhood, especially with reference to case reports. Bradley suggests that, as the pediatric services in most hospitals limit the age to 12 or 13 years, this age period be accepted as the limit of childhood in descriptions of psychiatric cases. JAHR, Omaha.

SIGNIFICANCE OF SPECIAL READING DISABILITY IN MENTALLY HANDICAPPED PROBLEM CHILDREN. T. G. HEGGE, Am. J. Psychiat. **94**:77 (July) 1937.

At least 10 per cent of the public school population suffers from special disability in reading. This does not include those whose deficiency in this respect may be due to visual error or word blindness. It is obvious that such a defect may produce unfortunate end results not only scholastically but emotionally in the otherwise normal child and especially in the mentally handicapped youngster, who is already struggling under social and academic maladjustment. Approximately

90 per cent of high grade morons may be expected under present day methods of instruction to develop a reading ability corresponding to their mental age. By the time they leave school they will have acquired a fourth grade ability to read. Although education of the mentally handicapped must stress recreational and vocational activities, social and cultural values cannot be entirely neglected. Most of these children are trainable. Furthermore, progress in reading is often accompanied by improvement in other subjects.

Reading disability is discussed in its relationship to maladjustment, as is special treatment of this disability as a therapeutic adjuvant. Two illustrative cases are presented. In the borderline cases correction of reading disability is not as difficult as it would appear.

JAHR, Omaha.

EFFECT OF BENZEDRINE SULFATE ON THE INTELLIGENCE SCORES OF CHILDREN. M. MOLITCH and A. K. ECCLES, Am. J. Psychiat. **94**:587 (Nov.) 1937.

Ninety-three boys varying in age from 11 to 17 years and of varying mental levels were examined with a battery of tests before and after medication with benzedrine sulfate. One-half the number received a placebo tablet which in appearance resembled the tablet of benzedrine sulfate given to the other group, for the purpose of eliminating the factor of suggestion. While both groups showed improvement in the retest, the children receiving the drug averaged higher than those receiving the placebo.

JAHR, Omaha.

PRIMARY AFFECT HUNGER. D. M. LEVY, Am. J. Psychiat. **94**:643 (Nov.) 1937.

This paper deals with a discussion of emotional hunger for maternal love and those other feelings of protection and care implied in the mother-child relationship. Maladjustments of varying degrees may be grouped in three classes as due respectively to (1) extreme deficiency (abandonment or neglect because of social or economic inconveniences, broken homes and the like) from infancy extending through early childhood; (2) partial or complete rejection following a favorable relationship in infancy and early childhood, due to altered circumstances in the home, and (3) strain in the parent-child relationship, based on early oversolicitude followed by an attempt to improve the misguided attitude in this relationship. The first group presents a chronic condition of emotional starvation with a poor prognosis. The second two groups respond favorably in many cases to psychotherapy and social aid.

JAHR, Omaha.

DEFECTS OF INTELLIGENCE FROM FOCAL LESIONS WITHIN THE CENTRAL PART OF THE CEREBRAL HEMISPHERE. L. B. ALFORD, Am. J. Psychiat. **94**:651 (Nov.) 1937.

A clinical and pathologic study of 7 cases of hemiplegia is presented. Intellectual defects, when present, the author postulates, must be explained not so much by the nature and extent of the lesion as by the structures directly or indirectly affected by the lesion. Evidence is submitted from postmortem studies that at the present time too great reliance is placed on the cortex in connection with mental processes and related functions.

JAHR, Omaha.

AN EVALUATION OF THE TREATMENT OF PROBLEM CHILDREN AS DETERMINED BY A FOLLOW-UP STUDY. H. W. POTTER and H. R. KLEIN, Am. J. Psychiat. **94**:680 (Nov.) 1937.

One hundred seventy-five children, who formerly had been inpatients of the New York State Psychiatric Institute and Hospital and who had been dismissed from the hospital one or more years, were followed up through various reliable

channels. This large class was divided diagnostically into groups and the results of the follow-up rated as satisfactory or unsatisfactory, depending on the nature of their adjustment:

	Satisfactory	Unsatisfactory
1. Organic reaction groups		
(*a*) Idiopathic epilepsy, 9 cases	3	6
(*b*) Mental deficiency, 27 cases	5	22
(*c*) Juvenile paresis, 7 cases	0	7
(*d*) Behavior problems secondary to organic conditions, 19 cases	2	17
2. Situational reaction groups		
(*a*) Personality and of habit, 25 cases	14	11
(*b*) Disorders of conduct, 51 cases	26	25
(*c*) Psychoneuroses, 21 cases	15	6
3. Schizophrenia, 14 cases	1	13

JAHR, Omaha.

PROBLEM CHILDREN GROWING UP. L. KANNER, Am. J. Psychiat. **94**:691 (Nov.) 1937.

Seventy-five children, 43 boys and 32 girls, 70 white and 5 colored, were all studied and followed up for between four and six consecutive years. The best response to treatment was found where there existed a combination of intelligence (filial and parental), sound ancestry, tolerable housing conditions and school and communal cooperation and facilities. The more of these features that were absent the less gratifying were the results. Yet at times much could be done for a child even when parental understanding and cooperation were lacking and the general environmental conditions did not change appreciably.

JAHR, Omaha.

SCHIZOPHRENIA IN A CHILD. L. RESNIKOFF, J. Nerv. & Ment. Dis. **85**:262 (March) 1937.

A colored boy aged 9 years with a negative developmental history was brought to the clinic with the complaint that for about a year he had been showing personality changes. He would not talk to any one at home but talked to himself for hours at a stretch. He had hallucinations, auditory and visual. Examination showed typical evidence of schizophrenia. The psychotic symptoms subsided in about six months. The psychosis reappeared at the age of 13 years with the death of his godfather, to whom the patient had been much attached. At the time the report was made the boy was under treatment, and the condition seemed to be subsiding.

JAHR, Omaha.

EFFECT OF HEAD INJURY ON THE BEHAVIOR AND PERSONALITY OF CHILDREN: A STUDY OF TWENTY CASES. H. W. NEWELL, M. Clin. North America **21**:1335 (Sept.) 1937.

In his study of 20 children with disturbance of behavior or personality following an injury to the head, Newell found 10 with neurotic symptoms, 5 with delinquent behavior, 4 given to explosive tantrums and 5 who were mentally retarded. The mental retardation was found to be functional, no organic deterioration being detected by psychologic tests. In 3 cases the Stanford-Binet test gave the same result before and after injury.

The effect of injury of the brain seemed to be a diffuse increase of irritability with a general decrease of inhibitory functions. In the realm of behavior and personality, the result was in no sense specific, and there was little correlation between the changes in behavior and the severity of the injury to the head.

An important factor, however, was the emotional attitude of the parents to the injury, especially when damage suits were threatened or pending. The most effective therapy was direct psychiatric treatment of the patient and advice to the parents as to the proper methods of handling the child.

EUGENE H. SMITH, Ogden, Utah.

SOME BEHAVIOR PROBLEMS MET WITH IN PEDIATRIC PRACTICE. H. SCHUMACHER, M. Rec. **146**:116 (Aug. 4) 1937.

Schumacher takes up separately the following problems of behavior and discusses them: (1) unsatisfactory feeding, (2) disturbances of sleep, (3) thumb sucking, (4) nail biting, (5) enuresis, (6) masturbation and (7) mental retardation.

Lastly he points out the difficulties that may arise during convalescence after a severe illness. During the illness the child has become highly egocentric. At the time everything must be done for the child, but during convalescence the child should be allowed to do more and more for himself. A sensible handling of this stage in recovery would prevent many problems in the behavior of children which are due to overprotection and oversolicitude on the part of the parent as well as to the use by the child of his former symptoms to obtain his way through conversion of these symptoms into those of hysterical illness.

WILLIAMSON, New Orleans.

"ARRESTED" MENTAL DEVELOPMENT. M. H. ERICKSON, M. Rec. **146**:352 (Oct. 20) 1937.

Two cases, one of complete and another of partial mental arrest, are presented, with a discussion of each. Each child was seen by at least four psychometrists, who concurred in their observations. The first patient was tested from the age of 11 years to that of 16 years, uniformly showing in these examinations that the mental age was 8 years 10 months by the Binet-Simon test.

The second was followed from the age of 6 years 4 months to that of 16 years 9 months and showed a mental age of from 3 years 10 months to 5 years 4 months.

WESTON JR., Columbia, S. C.

CHARACTER CHANGES AND SOCIAL INADAPTATION AMONG CHILDREN OF MIXED RACIAL STRAINS. G. HEUYER and F. LAUTMANN, Arch. de méd. d. enf. **40**:553 (Sept.) 1937.

At a recent international conference on eugenics, held at Scheveningen, Holland, the problems resulting from intermarriage among nationals of different races were given consideration. It was pointed out that the French societies, particularly, had made no significant contributions in this field, although the opportunities afforded in the colonies were apparently most abundant.

The present paper is offered in acknowledgment of this challenge and in the hope that further studies may be made in families of mixed races—for example, the offspring of French and Chinese, French and Antillean, or Negro and East Indian parentage.

The authors report 10 observations on children of such families, selected at random in the neuropsychiatric clinic and brought to the hospital more for irregularities of behavior than for mental retardation. These children ranged in age from 5 to 12 years; all showed antifamilial or antisocial reactions, and the older members of the group, 6 in number, had been frequently under restraint for minor crimes or vagabondage. Among these subjects there were 3 who were proved to have hereditary syphilis and 2 in whom syphilis was probable.

AMESSE, Denver.

FEAR OF DEATH AND THE DEATH INSTINCT: A NEUROTIC MECHANISM. EDWARD HITSCHMANN, Ztschr. f. Kinderpsychiat. **3**:165 (March) 1937.

The fear of death, the wish to die and the impulse to kill are neurotic manifestations of the feeling of guilt. The psychoanalytic implications are illustrated in 3 cases cited in the paper.

JAHR, Omaha.

BEARING OF THE CHVOSTEK SIGN ON THE MENTAL ASPECTS OF THE CHILD. M. SCHACHTER, Ztschr. f. Kinderpsychiat. **4**:1 (May) 1937.

The Chvostek sign has long been recognized as an indicator of nerve irritation (spasmophilia, tetany), and most of the studies dealing with the phenomenon pertain to the physiologic phases of this sign. Schachter examined 1,158 school children. Of these, 119 presented the Chvostek sign, varying in degree and intensity. In their adjustment to their surroundings they did not differ materially from their fellows who did not present this sign. The conclusion is reached that, while the sign indicates nerve irritability, few of the children observed in this study, at least, may be looked on as nervous, inattentive or hyperactive.

JAHR, Omaha.

WORD-BLIND CHILDREN. P. A. HANSEN-SCHWALBE, Ugesk. f. læger **99**:520 (May 13) 1937.

Dyslectic children should be examined and tested mentally very carefully, as their abnormality may simulate psychic deficiency. Their intelligence quotient is comparable to that of normal children. Not only their reading difficulties should be treated (special classes) but also their psychic disturbance (inferiority complex).

WALLGREN, Göteborg, Sweden.

Diseases of Genitourinary Tract

WHAT IS LIPEMIC NEPHROSIS? G. FAHR, Am. J. M. Sc. **194**:449 (Oct.) 1937.

"Chronic genuine nephrosis (lipemic nephrosis)" is the term used by Fahr to differentiate a distinct disease which is a part of the usual picture of subacute and subchronic glomerulonephritis. The signs and symptoms of lipemic nephrosis are only a part of the picture of glomerulonephritis but occasionally become so prominent that when associated with an absence of hypertension and hematuria they seem to represent a distinct clinical and pathologic entity.

HENKE, Omaha.

THE NEPHROSES. A. EPSTEIN, Bull. New York Acad. Med. **13**:621 (Nov.) 1937.

This is a comprehensive review covering present knowledge of the nephroses. The clinical and laboratory phases of this group of renal diseases are discussed in the light of the pathologic changes involved. The term "nephrosis," Epstein states, represents in reality a compromise between the pathologist and the clinician. The etiologic background, symptoms, course, treatment and prognosis are discussed in detail.

JAHR, Omaha.

LATE EFFECTS OF ACUTE PYELITIS IN GIRLS. L. R. WHORTON, L. A. GRAY and H. C. GUILD, J. A. M. A. **109**:1597 (Nov. 13) 1937.

Thirty girls who had been hospitalized for pyelitis were given nonoperative urologic examinations about ten years, on the average, after their last attack of pyelitis in childhood. Only 2 were in poor health resulting from renal disease, and the remainder had no complaints to offer, although some, on being questioned, affirmed that they had noted symptoms. However, 17 of the group (57 per cent) were found to have definite abnormalities of the urinary tract of some type. The authors advise that follow-up studies be made several months after a urinary infection in childhood has cleared symptomatically.

HEERSMA, Kalamazoo, Mich.

NONOBSTRUCTIVE DILATATIONS OF THE UPPER PART OF THE URINARY TRACT IN CHILDREN. A. B. HEPLER, J. A. M. A. **109**:1602 (Nov. 13) 1937.

Hepler discusses the causes of dilatation of the upper part of the urinary tract in children. He describes the dynamics of the ureteral functions and dysfunctions, particularly of the autonomic nervous system, and presents 4 cases of the type in which no mechanical obstruction and no central or peripheral lesions are found. In each case there were a relaxed ureteral orifice, loss of tone in the meatus and the adjacent trigon of the bladder, disturbance in the function of the meatus, as seen in the cystoscopic examination, and chronic dilatation of the upper part of the tract. The condition is comparable to Hirschsprung's disease of the colon, which was present in 1 of his cases. Treatment will be directed to the intrinsic sympathetic nerves and their controlling ganglions when their functions have been more completely determined. HEERSMA, Kalamazoo, Mich.

PRIMARY MALIGNANT TUMORS OF THE UROGENITAL TRACT IN INFANTS AND CHILDREN. M. F. CAMPBELL, J. A. M. A. **109**:1606 (Nov. 13) 1937.

In discussing the types of malignant tumors of the adrenal gland, kidney, bladder, testis, penis and urethra in infants and children, Campbell stresses diagnosing these conditions early by urography, biopsy of aspirated material and hormonal tests in order to reduce the high mortality. He describes and emphasizes the importance of preoperative and postoperative fractional irradiation, employed along with judicious surgical intervention. HEERSMA, Kalamazoo, Mich.

A CLINICAL EVALUATION OF THE HORMONE TREATMENT OF CRYPTORCHIDISM: AN ANALYSIS OF THIRTY-NINE CASES. J. H. HESS and R. H. KUNSTADTER, J. Pediat. **11**:324 (Sept.) 1937.

Of 39 persons with cryptorchidism treated by hypodermic injections of the gonadotropic substance from the urine of pregnant women, 28 (71.8 per cent) showed complete descent of the testes, bilateral in 25, unilateral in 3. Four (10 per cent) showed partial descent, bilateral in 1, unilateral in 3. Seven (18.2 per cent) failed to respond to the treatment; in 3 of these the condition was bilateral, and in 4 it was unilateral. Fourteen (36 per cent) of the patients were of normal constitution, and 25 (64 per cent) presented evidence of endocrine dysfunction of the hypopituitary type. The authors present a test to be used in determining the type of patient suitable for treatment. In normal young children a gonadotropic substance is excreted in the urine, showing normal activity of the anterior lobe of the pituitary and immaturity of the testes. As puberty approaches, the testes mature and the gonadotropic substance disappears from the urine. Bilateral cryptorchidism results physiologically in a phenomenon similar to castration; with the hypophysis functionally active, the circulating gonadotropic hormone is excreted in appreciable amounts in the urine. In cryptorchidism the testes eventually become atrophied and do not utilize all or any of the circulating hormone. The absence of the gonadotropic factor in the urine of a person with bilateral cryptorchidism signifies that there is a primary insufficiency of pituitary function, and the presence of this factor indicates that the pituitary is normal and that the testes are still functionally unable to utilize the gonadotropic factor. Primary insufficiency of pituitary function may usually be determined from clinical and laboratory evidence. In unilateral cryptorchidism the urine usually lacks the gonadotropic substance, as one normal testis is adequate to utilize the available circulating substance. This signifies that a mechanical obstruction and not a lack of circulating gonadotropic hormone is the cause of the cryptorchidism. In many of these cases treatment with gonadotropic substance would not give satisfactory results. The determination of the amount of gonadotropic substance in the urine will in many cases indicate whether there is adequate secretion of the hormone by the pituitary gland, to what extent the testes are functioning and what may be expected from treatment with gonadotropic preparations. RAUH, Cincinnati.

THE TREATMENT OF ACUTE NEPHRITIS AND ITS COMPLICATIONS IN CHILDHOOD. T. C. GOODWIN, M. Clin. North America **21**:1379 (Sept.) 1937.

The acute nephritis referred to in the title is the condition also known as acute glomerular nephritis, acute hemorrhagic nephritis and acute diffuse nephritis. Since this disease is secondary to acute infection elsewhere in the body, treatment begins with the treatment or elimination of the infection. The organism most frequently implicated in acute nephritis is the hemolytic streptococcus. Severe streptococcic infections should be treated with available specific serums and sulfanilamide. The latter agent apparently does not injure the kidney and may be used even during the presence of nephritis. Dosage, however, should be controlled by frequent examinations of the blood to avoid too great concentration in the blood stream.

Diet in acute nephritis should be light and nutritious, with sodium chloride reasonably limited. When the loss of protein is excessive, resulting in abnormal lowering of the blood protein, the protein in the diet should be increased, especially if edema is present. A middle course in regard to fluids is advised, and close to a normal intake is allowed. The most valuable drug in the treatment of acute nephritis is magnesium sulfate, which is given to almost all of the author's patients, by mouth, by rectum or into the muscle. Nervous complications, including coma and convulsions, are best controlled by this medication. Occasionally lumbar puncture may be done to relieve acute intracranial tension but only with extreme caution. Myocardial failure was present to some extent in about 15 per cent of the patients of this type admitted to the hospital. The hypertension usually present is combated by means of magnesium sulfate. Hypertonic dextrose administered by vein is of great value. Digitalis may be given, but cautiously, since diminished renal function predisposes to toxic action of the drug. Oxygen gives great relief to the cyanotic child. A failing heart demands the use of all remedies of tried and proved worth.

EUGENE H. SMITH, Ogden, Utah.

SIGNIFICANCE OF GLOMERULAR NEPHRITIS IN CHILDHOOD. J. M. BIERMAN, Minnesota Med. **20**:703 (Nov.) 1937.

Bierman reviews work done by Addis and Snoke and also work done by herself in cases of glomerular nephritis, using the Addis technic, and concludes that with the ordinary methods used in examination of urine many children who have been thought completely recovered have had a latent form of the disease which over a long period of years may even go on to advanced stages. Bierman feels that the most important treatment of glomerular nephritis is rest of the kidney. This is best obtained during acute infections by administering large amounts of fluids, by eliminating known irritants from the diet and by avoidance of irritating diuretics. A normal intake of protein should be maintained, and for protein lost in the urine additional protein to the same amount should be given in the diet. The blood pressure should be taken frequently. If toxic symptoms arise, magnesium sulfate should be given intravenously and by mouth. Patients should be allowed a long period of convalescence. During the late stage, foci of infection should be cleared up. A full, balanced diet is given and the child allowed to lead as nearly as possible a normal life.

ANDERSON, Minneapolis.

USE OF YOLK-MILK IN ACUTE NEPHRITIS IN CHILDREN. F. CHUBACHI and C. NAKAMURA, Acta pædiat. japon. **43**:1261 (Aug.) 1937.

The authors report the favorable effect of yolk-milk (Chubachi) as a diet in the treatment of acute nephritis uncomplicated by uremia. This mixture is prepared as follows: Mix 4 Gm. of corn starch or rice powder in 200 cc. of water and bring to a boil. In another bowl mix the yolk of an egg, 10 Gm. of sugar and 0.2 Gm. of calcium lactate. Then while it is still warm stir the boiled starch water slowly into the egg yolk mixture. The two are thus thoroughly mixed.

This mixture, known as yolk-milk mixture, is somewhat deficient in vitamin C, which must be supplied by other appropriate means. The authors successfully used this mixture as a diet in all uncomplicated cases of acute nephritis.

KATO, Chicago.

GIANT HYDRONEPHROSIS IN AN INFANT OPERATED ON SUCCESSFULLY. H. ABRAHAMSEN, Ugesk. f. læger **99**:879 (Aug. 26) 1937.

An infant 8 months old with a large congenital hydronephrosis was successfully operated on in two sittings, first nephrostomy with emptying of the hydronephrotic sack, then nephrectomy.

WALLGREN, Göteborg, Sweden.

KETOGENIC DIET IN THE TREATMENT OF CHRONIC PYURIA. S. M. LAMMERTS VAN BUEREN, Maandschr. v. kindergeneesk. **6**:497 (Sept.) 1937.

Lammerts van Bueren publishes his experience with a ketogenic diet in 7 children from 3½ to 7 years of age who were suffering from chronic pyuria, which was resistant to any medicinal treatment. In 1 of the cases a complication made a suspension of the diet necessary; in all the other cases the urine became sterile after from four to eleven days. Examination of the children two years after this treatment showed that 2 of them suffered again from pyuria; the other 4 had been in good condition.

VAN CREVELD, Amsterdam, Netherlands.

RELATION BETWEEN THE ACIDITY OF THE URINE AND THE FORMATION OF RENAL AND VESICAL STONES. A. POLAK and A. PIET, Nederl. tijdschr. v. geneesk. **81**:5529 (Nov. 13) 1937.

In continuation of earlier studies of the connection between diet and the formation of renal or vesical stones, a more detailed investigation was made of the urinary acidity in animals kept on the diets used in these studies. It was shown that the urine of animals kept on a diet containing 3 per cent calcium carbonate had nearly constantly a p_H over 7. When the calcium carbonate was replaced by calcium chloride, the p_H was always below 7. Rats which were given 13 per cent calcium gluconate instead of 3 per cent calcium carbonate showed marked variability of the urinary p_H. Addition of 3 per cent sodium benzoate appeared to have little influence on the p_H of the urine of rats kept on a stone-producing diet, so that the stone-preventing action of these small quantities of sodium benzoate will have to be explained in another way.

VAN CREVELD, Amsterdam, Netherlands.

Diseases of the Ductless Glands; Endocrinology

EFFECT OF GRADED DOSES OF ESTRIN UPON THE PITUITARY, ADRENAL, AND THYMUS WEIGHTS OF MATURE OVARIECTOMIZED RATS. H. LAUSON, C. G. HELLER and E. L. SEVERINGHAUS, Endocrinology **21**:735 (Nov.) 1937.

A twenty day period of castration did not change the average pituitary and adrenal weights of mature female rats but led to marked hypertrophy of the thymus, which averaged 60 and 100 per cent above normal levels in two series.

Daily injection of estradiol following castration caused distinct pituitary hypertrophy, did not alter adrenal weights and prevented castration hypertrophy of the thymus. Large doses (62.5 rat units) caused atrophy of the thymus.

Gain in weight followed castration; this was progressively less with increasing doses of estrogen, and with large doses there was only a slight loss of weight.

JACOBSEN, Buffalo.

EXCRETION OF ANDROGENIC AND ESTROGENIC SUBSTANCES IN THE URINE OF CHILDREN. R. I. DORFMAN, W. W. GREULICH and C. I. SOLOMON, Endocrinology **21**:741 (Nov.) 1937.

The urine of 18 boys and 5 girls, ranging in age from 6 to 16 years, were assayed for androgenic and estrogenic activity. The androgenic activity indicated an excretion of from 1.1 to 32 international units per twenty-four hours, while the estrogenic activity indicated a range of from less than 5 to 95 international units for the same period. Attention is called to the difference in excretion of gonadotropic substances in children who, though of the same chronologic age, differ from each other in the degree of their physical maturity.

JACOBSEN, Buffalo.

TESTOSTERONE AND TESTOSTERONE ACETATE AND THE PROTEIN AND ENERGY METABOLISM OF CASTRATE DOGS. C. D. KOCHAKIAN, Endocrinology **21**:750 (Nov.) 1937.

Testosterone and testosterone acetate cause retention of nitrogen but do not affect the energy metabolism of castrate dogs. The results in both cases are similar to those obtained in previous studies with urinary androgenic extracts and androstenedione.

JACOBSEN, Buffalo.

EFFECT OF THYROGLOBULIN AND RELATED SUBSTANCES ON THE O CONSUMPTION OF LIVER IN VITRO. A. CANZANELLI and D. RAPPORT, Endocrinology **21**:779 (Nov.) 1937.

The effect of certain substances on the O consumption of guinea pig and rat liver in vitro has been studied, with the following results: Thyroxin had no effect on either tissue, while thyroglobulin (hog) markedly increased the O consumption of both. Di-iodothyronin was inconstant, occasionally either raising or depressing the O consumption but usually having a negligible effect. Except for a few instances of depression, thyronin had no effect. Di-iodotyrosin did not appreciably change the O consumption of guinea pig liver but consistently depressed that of rat liver. It is postulated that thyroxin is not the thyroid hormone and that the latter is either thyroglobulin or an integral part of it.

JACOBSEN, Buffalo.

PRESENT STATUS OF THE THYMUS PROBLEM: A REVIEW OF NONSURGICAL EXPERIMENTATION IN THIS FIELD. F. GUDERNATSCH, M. Rec. **146**:101 (Aug. 4) 1937.

Gudernatsch gives the outcome of recent investigations of the thymus gland by two groups of investigators. One group made their observations in 1929, in Asher's laboratory, and the other group, in 1933, in Rowntree's laboratory. In summing up he states that the physiology of the thymus, like the morphology of the thymus, still remains a fertile field for speculation. While derivatives of this gland administered to animals have been shown to produce a stimulating effect on their development, there is nothing yet in these experiments to justify the clinician in taking corresponding therapeutic measures in human patients. "Hypofunction" of the thymus has not yet been defined. Therefore, rational substitution therapy would be difficult, if ever called for.

WILLIAMSON, New Orleans.

A JUVENILE TYPE OF DIABETES: A STUDY SHOWING THE VALUE OF A HIGH CARBOHYDRATE CONTENT OF THE DIET. H. M. FEINBLATT and E. A. FERGUSON, M. Rec. **146**:293 (Oct. 6) 1937.

The juvenile diabetic patient is classed as one who is dependent on insulin, in contrast with the adult in whom dietetic measures overcome diabetes. The authors summarize their observations as follows:

"The relative sensitivity of the individual to insulin is, to a large extent, dependent upon the carbohydrate-fat ratio of the diet.

"The caloric value remaining constant, the higher the carbohydrate-fat ratio, the greater is the sensitivity to insulin." WESTON JR., Columbia, S. C.

DIABETES IN CHILDHOOD. C. J. BLOOM, New Orleans M. & S. J. **90**:252 (Nov.) 1937.

This article is introduced by a short but interesting historical review. Congenital diabetes is rare, only 2 cases having been reported. Juvenile diabetes prior to 1900 was rarely recognized or at least rarely reported. It is now estimated to occur in 1 of every 8,000 children. This estimate indicates a total of about 25,000 diabetic or prediabetic children. More boys than girls are involved. Cities contribute a far larger percentage of these diabetic children than do rural districts. The racial distribution is still in dispute, but about 8 to 12 per cent of the patients are Jewish. Well to do children are more prone to the disease than the ones in moderate circumstances.

Trauma has been demonstrated to have produced both temporary glycosuria and diabetes. No definite relationship to diabetes in childhood has been shown in disturbance of the ductless glands, acute infection, syphilis, dietetic excess or obesity. The hereditary nature of diabetes is strongly supported but not proved. Bone changes occur in diabetes and can be demonstrated in roentgenograms.

The essentials of the treatment of diabetes in children are essentially the same as in adults. The important added factor is that some one and only one person must assume the responsibility for the observance of all rules and regulations. Diets are to be prepared which not only control the diabetes but furnish sufficient food for growth. Most children will exhibit normal growth on a diet which is two thirds of the normal for the age.

The partitioning of the diet and the use of insulin and protamine insulin are discussed. With modern methods of dietary control and the use of insulin, the expectancy of life in the diabetic child has been increased from two to between thirty-one and thirty-two years. BERKLEY, Los Angeles.

CUTANEOUS ABSORPTION OF INSULIN. R. H. MAJOR and M. DELP, Proc. Soc. Exper. Biol. & Med. **37**:338 (Nov.) 1937.

Major and Delp were able to show that cutaneous absorption of insulin occurs in rabbits and in patients independent of any abrasion of the skin. The amount absorbed by the cutaneous route, as shown by studies of the blood sugar, is variable and inconstant. HANSEN, Minneapolis.

"GLANDULAR" CELLS IN THE PARS NERVOSA AND STALK OF THE HYPOPHYSIS. I. GERSH, Proc. Soc. Exper. Biol. & Med. **37**:395 (Nov.) 1937.

Extensive histologic studies in rats of the possible glandular nature of the parenchymatous cells of the pars nervosa of the hypophysis lead to the conclusion that these cells produce and secrete an antidiuretic substance for the control of the water metabolism. These cells have been seen in almost every class of mammals and of pigeons and chickens. Histochemical analysis of the droplets or granules of these glands shows that in the rat they are rich in neutral unsaturated fats. When rats are on a dry diet, the glandular cells appear in greater number and size than the same cells in control animals. These changes revert to normal when the animals have access to water. These glandular cells are supplied with nerve fibers, which sweep in bundles down the hypophysial stalk. These cells seem to degenerate in severe experimental diabetes insipidus induced by section of the stalk of the hypophysis. HANSEN, Minneapolis.

THE LAURENCE-BARDET-BIEDL SYNDROME. R. AMYOT, Union méd. du Canada **66**:823 (Aug.) 1937.

The first case of the Laurence-Bordet-Biedl syndrome to be recorded in the Canadian literature is described by Amyot. The patient was 37 years old and had shown ocular signs from the third year. The second phalanges of the toes were absent, and the second phalanx of the fifth finger was shortened. Marked pigmentary retinitis was present. There was a family history of digital anomalies but not specifically of polydactylism or of syndactylism. Two aunts had been obese.

Menstruation was established at 15 years and had been normal. The patient had been pregnant three times, with a miscarriage each time.

DAFFINEE, Boston.

SPASMOPHILIA FROM THYROID HYPOFUNCTION. M. ACQUA, Méd. inf. **8**:354 (Nov.) 1937.

In children with tetany the amount of calcium in the blood returns to normal on the giving of thyroid. The hypothesis is advanced that hypothyroidism may be responsible for tetany in some cases.

HIGGINS, Boston.

PANCREOTOXIN TREATMENT IN DIABETES MELLITUS. G. P. SAKHAROFF and D. M. ROSSIISKY, Acta med. Scandinav. **93**:239, 1937.

Rabbits were immunized by injecting human pancreas obtained in cases of sudden death. The serum of these rabbits contained a species-specific toxin believed to be derived from the pancreas. The presence of this substance was proved by complement deviation.

A single subcutaneous injection of 0.1 cc. of this serum reduced the glycemic curve in normal persons by from 30 to 35 mg. per hundred cubic centimeters of blood. Fifty adults with diabetes were given from fifteen to forty daily injections of from 0.1 to 0.2 cc. of serum. No insulin or drugs were used. The general health and working capacity improved; the thirst and polyuria decreased. The blood sugar dropped from 325 to 135 mg. and from 250 to 80 mg. per hundred cubic centimeters of blood. Sugar disappeared from the urine or was present in traces only. The improvement lasted for a year; a second treatment proved similarly effective. The authors are not ready to report the results in juvenile diabetes.

KAJDI, Baltimore.

THE ADRENAL CORTEX SYNDROME. L. MEYLER and M. HOMMES, Acta med. Scandinav. **93**:253, 1937.

Two persons with hirsutism (hypertrichosis), obesity, an appearance of being older than they are and symptoms of virilism were treated by injections of ovarian preparations, with return to a normal appearance in both.

This syndrome is due to hyperfunction of the adrenal cortex, which may be secondary to eosinophilic and basophilic adenoma of the pituitary or to tumor of the thymus.

KAJDI, Baltimore.

PROTAMINE INSULIN. L. MEYLER and A. DE MAAR, Nederl. tijdschr. v. geneesk. **81**:4045 (Aug. 21) 1937.

Meyler and de Maar administered protamine insulin to 40 patients with good results. They wanted to reduce the number of injections to one daily, and in most of the cases they succeeded in doing so. In a few cases an injection of common insulin had to be given in the other thigh at the same time on account of the slow action of the protamine insulin; its action lasted at least twenty-four hours. The protamine insulin saves the patients much trouble, but regular polyclinical control of the patients given protamine insulin is still more desirable than that of diabetic patients who are getting the usual insulin.

VAN CREVELD, Amsterdam, Netherlands.

Skin Diseases; Allergy

DEFICIENCY OF ATMOSPHERIC HUMIDITY AS A CONTRIBUTING FACTOR IN PROLONGED ASTHMA. S. J. PARLATO, J. Allergy **8**:566 (Sept.) 1937.

Parlato compiled a group of readings of temperature and relative humidity taken in various indoor places during the months from Nov. 1, 1936, and March 1, 1937. The temperature ranged between 65 and 80 F.; the humidity, between 20 and 30 per cent.

Five patients who had had asthma continuously for from three days to two weeks responded to symptomatic treatment more readily and rapidly under improved air conditions. The moist air relieved the dry mucous membrane and aided in making the mucus less viscid and tenacious. It is felt that because of the dry membranes and sticky mucous preparations of belladonna and of stramonium and allied drugs are contraindicated.

HOYER, Cincinnati, Ohio.

BONE SCORINGS IN NORMAL AND ALLERGIC CHILDREN. R. CHOBOT and E. F. MERRILL, J. Allergy **8**:588 (Sept.) 1937.

Roentgenographic studies, made by using the technic of Todd, were carried out on a group of 17 allergic children and a group of 13 who had shown no sign of allergy. In the group of allergic children were 4 infants who had not walked, and in the control group were 6 children from the feeding clinic.

The authors conclude: "Our experience has shown that the so-called 'bone scorings' described by Todd occurred in the bones of a high percentage of children whether they suffered from allergic disturbances or not. Furthermore, they did not occur in all children who suffer from allergic disturbances. With these findings before us, we feel justified in drawing the conclusion that it is hazardous to diagnose the allergic state on the evidence presented by these 'bone scorings.'"

HOYER, Cincinnati.

ALLERGIC DISEASES IN CHILDHOOD. W. C. DEAMER, J. Allergy **8**:610 (Sept.) 1937.

This is a short but concise review of thirty-six articles in the literature pertaining to important aspects of allergic diseases of childhood.

The criticism of the conclusions reached in some of the reports is fair.

The article ends by citing London's note that 6.6 per cent of the patients in his practice sought relief from complaints of an allergic nature.

HOYER, Cincinnati.

ASSOCIATION WITH PSEUDOGLOBULIN OF THE SKIN SENSITIZING SUBSTANCE OF ALLERGIC (HAY FEVER) SERUM. A. STULL, W. B. SHERMAN and R. A. COOKE, J. Allergy **9**:7 (Nov.) 1937.

The skin-sensitizing substance from serums giving rise to allergy was associated specifically with the pseudoglobulin. Treatment of patients with pollen extract may cause a qualitative alteration in their serum pseudoglobulin rather than a significant quantitative change.

HOYER, Cincinnati.

SENSITIVITY TO HOUSE DUST AND GOOSE FEATHERS IN INFANTILE ECZEMA: ROLE OF SPECIFIC ALLERGENS. L. W. HILL, J. Allergy **9**:37 (Nov.) 1937.

A large proportion of infants under 1 year of age with atopic dermatitis are cutaneously sensitive to house dust and goose feathers. Normal infants are not likely to react to these two extracts. It may be that house dust or other environmental allergens are the cause of the dermatitis in some of the infants with more severe conditions who show no improvement on removal of all foods to which specific cutaneous sensitivity exists, but this has not been proved. The conclusion suggests itself that atopic dermatitis may persist in spite of a lack of exposure

to any allergen to which the patient is sensitive. This conclusion cannot be accepted until the influence of house dust, other environmental factors and possibly autogenous allergens have been more thoroughly studied.

HOYER, Cincinnati.

SERUM SENSITIVITY. J. H. BLACK, Texas State J. Med. **23**:312 (Aug.) 1937.

As a result of the increased use of serum as a therapeutic and later as a prophylactic measure, Black calls attention to the increased incidence of serum reactions. He classifies them into three types and claims that 90 per cent of all patients will show some reaction if a sufficiently large dose of serum is administered. He describes in detail the clinical symptoms of slight to fatal reactions. He points out the ease with which sensitivity can be detected by simple tests, easily made in the home, and explains in detail the methods of desensitization and of prevention of reactions.

MOORE, Dallas, Texas.

INFANTILE ECZEMA. H. M. MAYO, M. J. Australia **2**:914 (Nov. 20) 1937.

Mayo divides infantile eczema into an allergic (beginning on the face) and an infective (beginning on the scalp) type. In the allergic type the hereditary factor may be demonstrated in 60 to 70 per cent of the cases. Contributory, aggravating hereditary conditions may be ichthyosis and metabolic idiosyncrasies. Other predisposing causes are infection, especially in the type affecting the scalp, and dietary factors. The exciting causes, symptoms, diagnosis, prognosis and treatment (preventive and curative) of the two types are discussed fully along the usual lines.

GONCE, Madison, Wis.

INFANTILE ECZEMA. J. H. KELLY, M. J. Australia **2**:918 (Nov. 20) 1937.

Kelly presents an interesting review of clinical observations and experiences in the skin department of the Children's Hospital, Melbourne, Australia, during the last thirteen years. Speaking of the distribution and course of infantile eczema, he states:

"The capacity to react in this fashion is, I believe, an inborn characteristic which becomes manifest when stresses and strains oppress the individual. The child with infantile eczema shows failure of adaptation. Dentition is frequently delayed and the child may be slow to walk and talk. Some of these children reject all new foods when first given to them. When the child has adapted himself to his new environment—this world—the tendency to react disappears; but it may reappear with any subsequent disturbance in his life history, which is the result of maladjustment or a call for adaptation beyond his capacity."

GONCE, Madison, Wis.

EPIDERMOLYSIS BULLOSA HEREDITARIA IN TWINS. S. AHNSJÖ, Nord. med. tidskr. **14**:1883 (Nov. 13) 1937.

A pair of biovular twins had the dystrophic form of hereditary bullous epidermolysis. The father and his two brothers had had symptoms of the same disease at birth. In all cases the prognosis had been good.

WALLGREN, Göteborg, Sweden.

A SUGGESTION FOR REDUCING THE RISK OF ANAPHYLACTIC SHOCK AFTER INJECTIONS OF SERUM. B. BROMAN, Nord. med. tidskr. **14**:1943 (Nov. 27) 1937.

As a routine, serum from cattle should be used in prophylactic, and serum from horses in therapeutic, injections. Everybody who has received serum for either a therapeutic or a prophylactic purpose should receive a certificate as to the kind and amount of serum given, the mode of administration and the date of injection.

WALLGREN, Göteborg, Sweden.

Surgery and Orthopedics

Fractures of the Elbow in Children. I. Schulz, Wisconsin M. J. **36**:913 (Nov.) 1937.

Fractures of the elbow joints in children are extremely variable in type. Those of the lower end of the humerus are the most important from the standpoint of frequency and complications. Fractures involving one or more of the epiphyses of the lower end of the humerus may result in a change of growth causing deformity of the elbow and often limitation of motion. The various types of elbow fractures pose individual problems. Reduction must be careful, and often it must be of the open type. Roentgen examination and examination for nerve injury should be done before reduction is attempted. The reduction should be done with the patient under anesthesia.

The technic of reduction and the position of fixation are discussed. Careful watch should be maintained for seventy-two hours for signs of interference with the circulation and for Volkmann's ischemia. Flexion is maintained for fourteen days, and usually the arm is put in a sling in about twenty-one days.

In the treatment of a fracture of the head of the radius, the head should not be removed as it is in adults.

Supracondylar fractures should, because of the frequency of ischemic contractures, be treated as surgical emergencies.

Janney, Wauwatosa, Wis.

Teeth and Dentistry

Effect of Nutrition on the Primary Teeth. F. F. Tisdale, Child Development **8**:102, 1937.

To determine whether lack of vitamin D is a factor in tooth decay, 162 children living in an institution were divided into two groups and the diet, adequate except for vitamin D, was supplemented by vitamin D for one group, while the other group was maintained on the standard diet. Dental examinations were made at the beginning and at the end of the one year experimental period. The group given the diet deficient in vitamin D showed an incidence of dental caries in the deciduous teeth more than double that found in the group receiving the vitamin D supplement. Tisdale recommends the administration of a diet built around milk, meat, eggs, vegetables and fruit, with vitamin D added, and a comparatively low sugar content to decrease decay and insure normal healthy teeth.

[Angle Orthodontist.]

Some Biologic Aspects: Their Implications and Applications in Orthodontic Practice. Milo Hellman, Internat. J. Orthodontia **23**:761 (Aug.) 1937.

Hellman discusses the favorable and unfavorable influences of orthodontic appliances on the teeth and surrounding tissues. He believes the result frequently attained is normal occlusion, but whatever else happens, such an increase in size, change in form and alteration in position of the jawbones and the rest of the face is due to conditions over which mechanical devices have no influence and no control. He closes with the statement that while mechanics furnishes the means by which the possibilities of orthodontic practices are realized, biology reveals limitations within which such practices must be confined.

Lewis, Dayton. [Angle Orthodontist.]

Role of Nutrition as a Factor in Resistance to Dental Caries. May Mellanby, Brit. Dent. J. **62**:241, 1937.

Dental caries is not due to the absence or presence of any one factor. Yet experimental and clinical investigations suggest strongly that a deficiency of fat-soluble vitamins, especially of vitamin D, is the main single factor which

accounts for the prevalence of caries in temperate zones and is largely responsible for the comparative freedom from the disease of inhabitants of Arctic and tropical regions.

[ANGLE ORTHODONTIST.]

LATE RESULTS OF OPERATIVE TREATMENT OF CONGENITAL TORTICOLLIS. J. FOGED, Hospitalstid. **80**:8 (Nov. 30) 1937.

Foged examined 117 of 131 patients at from one to sixteen (average, five to six) years after operation. He considered the results in 86 per cent satisfactory, those in 11 per cent not quite good and those in 3 per cent bad (recurrence). The operation consisted in open tenotomy of the sternocleidomastoid muscle, combined eventually with excision of fibrous parts of the muscle and plastic elongation of the muscle. It should be done when the children are from 3 to 16 years old.

WALLGREN, Göteborg, Sweden.

Miscellaneous

SOME CAUSES OF MALNUTRITION IN INFANCY. C. L. JOSLIN, M. Clin. North America **21**:1275 (Sept.) 1937.

Uncomplicated malnutrition is a preventable disorder and may be controlled by proper modification of the diet to meet individual needs. When other factors enter the picture, the undernourished infant may present a difficult problem. As a preliminary to any attempts at treatment, a careful search for underlying causes should be instituted. The following outline is suggested by Joslin as a basis of study:

CAUSES OF FAILURE TO GAIN WEIGHT

I. Constitutional or organic conditions
  - Congenital abnormality, e. g., amyotonia congenita
  - Congenital heart disease
  - Defective cerebral development
  - Congenital anomalies

  Acquired conditions
  - Intracranial hemorrhage
  - Endocrine disorders

II. Infections
  - Parenteral: otitis media, mastoiditis, pyelitis, tuberculosis, syphilis
  - Enteral: diarrheal diseases, for example

III. Dietary deficiencies or faults
  - Quantity: insufficient or too many calories
  - Quality: incorrect formula

IV. Environmental influences
  - Home
  - Outside

Joslin discusses these various causes of malnutrition and cites illustrative cases. Rather striking are his reports of rapid gains following relief of intracranial pressure by lumbar puncture in cases of cerebral trauma sustained at birth, by operation in cases of "hidden mastoiditis" and by the feeding of fat-free milk in cases of fat intolerance.

EUGENE H. SMITH, Ogden, Utah.

SUDDEN DEATH DUE TO MERCURIAL DIURETICS. H. M. GREENWALD and S. JACOBSON, J. Pediat. **11**:540 (Oct.) 1937.

Two cases of death following the use of the mercurial diuretic neptal (an addition product of mercury acetate and salicylaminoallylacetic acid) are reported. The first case was that of a 2 year old white boy suffering from nephritis with

a nephrotic component. The first dose of neptal, 0.5 cc., was administered intramuscularly, with good diuresis. Five days later 1 cc. of neptal was given intramuscularly without beneficial results. One week later 1 cc. was injected intravenously and one minute later the child became dyspneic and cyanotic, the pupils dilated, the pulse became imperceptible, and the child died. Autopsy indicated that the condition causing death was probably an anaphylactoid one. The second case was that of a white boy 3 years old suffering from nephrosis. The first dose of neptal, 0.5 cc., was given intravenously, with good diuresis. Six days later the same amount was given intravenously. Three days later this injection was repeated and was followed in two minutes by a convulsion, coma, cyanosis and stertorous breathing. Oxygen, epinephrine hydrochloride intracardially and artificial respiration were employed, all without benefit. The patient died within five minutes after the injection. There was no autopsy. The authors discuss anaphylaxis or shock as the cause of death in these cases, quoting the evidence from the literature of anaphylaxis induced by chemicals. They emphasize the necessity of using small initial doses, of adhering to the same route of administration and of discontinuing the use of the drug when such danger signals as chills, elevation of temperature, malaise, morbilliform rash, headache, vomiting and convulsion occur.

RAUH, Cincinnati.

TOXICITY OF CERTAIN CODEIN COMPOUNDS FOR MALE AND FEMALE RATS OF DIFFERENT AGES. C. F. POE, J. G. STRONG and N. F. WITT, J. Pharmacol. & Exper. Therap. **61**:62 (Sept.) 1937.

It is frequently stated that morphine and its allied narcotics are more dangerous to the young than to the more mature human being. Therefore one conclusion of this work will be of interest to pediatricians: The toxicity of codeine does not vary with the age of the animal.

The only evidence for the prior statement that is recalled is that nurslings of certain animals are more sensitive to opiates than others.

PILCHER, Cleveland.

ANEMIA AND AGRANULOCYTOSIS DURING SULPHANILAMIDE THERAPY. G. H. JENNINGS and G. SOUTHWELL-SANDER, Lancet **2**:898 (Oct. 16) 1937.

When sulfanilamide and its derivatives were generally introduced, insufficient warning was given as to their possible toxic effects. These effects include cerebral disturbances, e. g., drowsiness, dizziness, headache and disorientation; alimentary disturbances, such as vomiting; irritation of the urinary tract, and disturbance of peripheral sensory nerves.

As is suggested by its chemical structure, para-aminobenzenesulfonamide is potentially poisonous to marrow; it may depress both erythropoiesis and leukopoiesis. Blood counts, whenever possible, should guide treatment. The appearance of immature erythrocytes or of leukopenia indicates that administration of the drug should be stopped.

LANGMANN, New York.

HEPARINISING THE DONOR IN BLOOD TRANSFUSIONS. P. HEDENIUS, Lancet **2**:1186 (Nov. 2) 1937.

This paper is based on the results of 150 transfusions carried out after heparin had been injected intravenously into the donors. This method has now replaced the citrate and whole blood methods in two Swedish hospitals. The method fulfils all the requirements of an ideal blood transfusion method, according to the author. It has all the advantages of the citrate methods and none of the disadvantages, such as a possible excess of anticoagulant when the expected amount of blood is not obtained.

A sterile 5 per cent heparin solution containing 0.25 per cent tricresol is injected intravenously (about 0.25 mg. per kilogram of body weight) into the donor, preferably into the arm that is not to be used in the transfusion. Ten minutes after the donor has received the heparin, the transfusion may begin.

LANGMANN, New York.

MISTAKES IN CALCULATING GAINS IN WEIGHT. R. DE LAMARE, Arch. de pediat., Rio de Janeiro **10**:81 (Nov.) 1937.

De Lamare presents some interesting calculations to prove that attempts to base opinions of weight gain on mathematical formulas are futile.

SANFORD, Chicago.

DIGITALIS THERAPY IN INFANCY. M. SLOER, Rev. Soc. de pediat. de Rosario **2**:170 (Sept.) 1937.

Digitalis is efficient when given by mouth in doses of 1 unit per 3 Kg. of weight. It is indicated in cases in which there are valvular defects of rheumatic origin, myocarditis and extrasystoles.

SANFORD, Chicago.

Society Transactions

AMERICAN PEDIATRIC SOCIETY AND SOCIETY FOR PEDIATRIC RESEARCH

Joint Meeting, Great Barrington, Mass., May 5-7, 1938

KENNETH D. BLACKFAN, M.D., *President*

HUGH MCCULLOCH, M.D., *Secretary*

First Session

Thursday Afternoon, May 5

PAST PRESIDENTS OF THE AMERICAN PEDIATRIC SOCIETY, 1888-1938: PRESIDENT'S ADDRESS. DR. KENNETH D. BLACKFAN, Boston.

This paper was published in the July issue of the AMERICAN JOURNAL OF DISEASES OF CHILDREN, page 1.

AMERICAN PEDIATRICS IN COLONIAL TIMES. DR. ERNEST J. CAULFIELD, Hartford, Conn.

This study is based chiefly on contemporary diaries, letters, church records, sermons and newspapers.

The length of the interval between epidemics partly explains why measles was so much more serious in America than in Europe. The early epidemics were about thirty years apart (1657, 1687, 1713), but by the early part of the nineteenth century the interval was about five years. Consequently, measles in colonial times was a disease of adults as well as of children, and it was frequently fatal in adults. There is some fragmentary evidence that encephalitis was a frequent complication during the epidemic of 1687.

Whooping cough often caused alarming hemorrhages. During the seventeenth century, it was called "The bloodye Coffe," and children were described as "coughing casting constraining and bleeding at ye Nose & Mouth."

Because of the frequency of the epidemics and the high case fatality, bacillary dysentery was a frightful disease in colonial times. It frequently caused the deaths of 2 or 3 and sometimes as many as 6 children in a family within two weeks; it not infrequently was fatal within forty-eight hours of the first symptom. Most of the deaths occurred in August, September or October. During the Revolution, dysentery was carried into many towns by infected soldiers.

Sporadic diphtheria was present after 1659. In 1735 malignant diphtheria broke out in New Jersey and New Hampshire, and it subsequently spread through most of the colonies. This was the most horrible epidemic of a children's disease in American history. In some towns half of all the children died, and in New England (population 222,000) there were approximately 5,000 deaths. Though this was supposed to have been a new disease, the age distribution of immunity was similar to that of today.

Scarlet fever appeared in Boston in 1702 and during the early part of the eighteenth century; the case fatality was less than 5 per cent. After the Revolution the disease was more malignant. Neither scarlet fever nor diphtheria was supposed to be contagious. They were considered as different manifestations of the same disease.

The infant mortality late in the eighteenth century was about 120 per thousand. Artificial feeding was only occasionally mentioned, and cholera infantum did not seem to cause much concern until the time of the Revolution. "Convulsion fitts" was the most common cause of death in the neonatal period. Wet-nurses frequently advertised in the newspapers, and baby farming was practiced extensively in New England. Rickets was overlooked, but rachitic tetany seems to have been common. Infanticide is occasionally found in the records of the period previous to 1740.

About 35 per cent of all deaths were in the group of children under 5 years of age. The spread of tuberculosis was aggravated by colonial living conditions. Most of the children had worms.

The colonial surgeons were skilful in repairing harelip and in trephining fractured skulls. The most frequently mentioned operation was "cutting for the stone."

The most common accidents of children were fractures of the skull (playing in the streets), burns (open fireplaces, candles, gunpowder), scalds (falling into large open kettles of boiling milk, water, chocolate and wort) and drownings (falling into unprotected wells).

EXPERIMENTS AT LOW NITROGEN PRESSURE. DR. JAMES L. WILSON, DR. ALLAN M. BUTLER, DR. CLEMENT A. SMITH (by invitation), DR. SIDNEY FARBER (by invitation), DR. L. SHAW (by invitation) and DR. PHILIP DRINKER (by invitation), Boston.

Preliminary experiments have extended the observations of Paul Bert and J. S. Haldane concerning the influence of low nitrogen pressures on the physiologic effect of the oxygen in inspired air. The effects of helium-oxygen atmospheres on respiratory obstruction have been compared with those of low nitrogen, normal oxygen atmospheres of comparable densities.

The data present the effects of different atmospheres (1) on the intrapulmonary pressure reflexly established in breathing with an obstruction which simulates obstruction of the upper respiratory tract, and (2) on the composition of the alveolar air and of the minute volume of inspired air resulting from definite intrapulmonary pressures established by voluntary control of respiration.

Observations on the effect of low nitrogen pressures on the concentration of nitrogen in the blood, on the occurrence of bends during the rapid reduction of atmospheric pressure and on combustibility are also presented.

DISCUSSION

DR. JOSEPH STOKES JR., Philadelphia: I should be interested in knowing if Dr. Wilson has treated patients who have obstruction due to laryngitis. For the past few winters my associates and I have had experience somewhat similar to Dr. Barach's with 80 per cent helium and 20 per cent oxygen in a tank with an internal circulation developed by Dr. Charles Chapple. We have not had enough cases to determine the value of this mixture in treatment, although there has been marked relief in some cases. In cases of obstructive laryngitis the difficulty lies in the fact that if the patient becomes worse immediate operation has to be performed. As the patient is removed from the tank situations requiring operation may occur when facilities for it are not available. It seems to me that this method does open real possibilities in the treatment of obstructive conditions.

DR. ALLAN M. BUTLER, Boston: I shall answer Dr. Stokes' question. We compared the effects of helium atmospheres with those of our low nitrogen, low pressure atmospheres. Using an atmosphere combining 25 per cent oxygen, 10 per cent nitrogen and 65 per cent helium, we have observed marked diminution in respiratory effort in the presence of obstruction of the upper respiratory tract.

We get, however, a little better ventilation with our low nitrogen, low pressure atmosphere than with such a helium atmosphere. On the other hand, in the low pressure atmospheres the partial pressures of water vapor and of carbon dioxide infringe on the available pressure of oxygen in the alveolar air and therefore require the use of a higher pressure of oxygen to keep the blood oxygenated. This is a definite disadvantage as compared with the effect of helium.

Relatively little attention has been called to the development of bends in experiments done at low pressures. Von Schrötter mentioned symptoms similar to those of bends but ruled out its occurrence as theoretically unlikely. Bert and Haldane mentioned the theoretic possibility of its occurrence. But neither they nor Schneider and his co-workers have mentioned that they encountered it. We were therefore surprised when we realized that it is a real trouble and something we have to think of constantly. Since equilibrium with a changing nitrogen environment is accomplished through the lungs, we have been cautious in the treatment of patients who have respiratory difficulty by means of low nitrogen, low pressure atmospheres until we have thoroughly studied the physiology of respiration under such conditions.

Dr. James L. Wilson, Boston: We have not treated any seriously ill patients in this chamber, partly because none was available and partly because we wished first to carry on more physiologic experiments. I do not believe that caisson disease is going to be a serious problem in this work. It is easy to prevent.

Dr. Stokes mentioned that the great trouble with helium is the leakage and, of course, the expense. The expense of the oxygen used in the chamber is far less, and little of the gas is wasted.

Controlling the External Environment of Premature Infants in an Incubator. Dr. Charles C. Chapple (by invitation), Philadelphia.

In an attempt to solve the problem of cross infection at the Children's Hospital of Philadelphia, an incubator was built to circulate outdoor air. Ward air is excluded from the chamber containing the infant by (1) handling the baby through balloon cloth sleeves through which only the hands are inserted; (2) admitting bottles and diapers through an air lock which prevents the entrance of any current of ward air, and (3) maintaining a small positive pressure inside the chamber so that in any leakage which may take place air will pass from the chamber and not into it. In this incubator any desired temperature and humidity can be held with slight fluctuation, and special mixtures of gases, such as those with high oxygen concentrations, can be maintained.

An incubator was installed in a fifteen bed ward of sick older infants, where cross infections were constantly occurring. The incubator attendants wore no masks or gowns but were careful to wash the hands before inserting them through the sleeves.

Under these conditions bacterial counts were taken by the Wells method of centrifuging the air against agar tubes. The ward air counts varied from 400 to 1,100 bacterial colonies per tube (representing 5 cubic feet [0.14 cubic meter] of air); the outdoor air, from 20 to 40 colonies, and the incubator air, from 2 to 20 colonies. The incubator was unoccupied when the tests were made, but it had been in the ward for one year and had been cleaned two weeks previously, when the last occupant was removed. The mechanism had been functioning for two hours, and it was maintaining a temperature of 90 F. and a relative humidity of 70 per cent.

Similar tests were made on an occupied incubator in the nursery of a maternity hospital, where the air in the ward averaged 90 colonies per tube and the outdoor air 23 colonies. The incubator in this ward averaged 9 colonies per tube.

While the total number of infants cared for in the incubator is not yet great enough (10 in the Children's Hospital and 16 in maternity departments of other

hospitals) to be conclusive evidence in favor of this method of caring for the premature baby, the evidence so far has been favorable. No infection of the respiratory tract has occurred in any infant in an incubator, and there has been only 1 case of transitory diarrhea, while in a control group of similar size under strict isolation at the Children's Hospital there were 4 cases of fatal pneumonia and 1 of fatal diarrhea. The only death caused by infection in an incubator resulted from septicemia originating in an abscess at the site of repeated hypodermoclyses.

Cyanotic attacks were reduced in number by the use of high humidity and high oxygen concentration.

The diurnal fluctuation of temperature as recorded rectally was seldom as great as 1 degree F. Since the temperature is held so exactly to the desired level, the babies are left uncovered and unclothed. Thus they are free to exercise, which they do to a remarkable degree, and their respiration is unhampered by the weight of blankets.

Continuous observation of the baby in the nude state is permitted.

DISCUSSION

Dr. Allan Butler, Boston: I wonder if Dr. Chapple would tell the members the cost of the units. It seems that this is obviously the best way to handle babies.

Dr. Charles C. Chapple, Philadelphia: Each unit has so far cost about $500, which is, when compared to the cost of air conditioning, really rather low.

Dr. Charles H. Smith, New York: Last summer when I got back from my vacation, I found that the incubators in the hospital with which I am associated were not working. They are of the Morgenthal type, cost about $400 apiece and are used extensively in hospitals, I believe. They are efficient in preventing great fluctuations of temperature. But when these incubators stopped working the infants' temperatures showed wide variations. The hospital engineer said that the incubators were all right; the manufacturer's representative said they were all right, and still the incubators did not work. Another engineer found that there was no difference between the air in the ward and that in the incubator. Some one had ordered the temperature of the ward air changed from 75 to 80 F., and since the thermostats in the incubators were set for 80 F., the lights were not turned on. They work only when set 5 degrees above the temperature of the room in which they are used.

Dr. Joseph Stokes Jr., Philadelphia: There are certain points about this incubator that I think should be emphasized. Dr. Chapple has had an interesting experience with twins placed in the same incubator. The temperature of these twins continuously differed by 2 degrees. It appears essential that each premature infant should have his own regulation, which is possible with this method.

So far as the nurses are concerned, no matter how well masks are made it is possible for bacteria or viruses to travel from the nurse to the infant inside the larger rooms, whereas in the incubator this is practically impossible. In this incubator there is a slight positive air pressure, which when the airlock is open assists in preventing bacteria from entering the incubator. In addition, it is possible to treat the outside air with direct ultraviolet radiation, which has proved effective in limiting the number of bacteria in the air.

Cystic Fibrosis of the Pancreas and Its Relation to Celiac Disease. Dr. Dorothy H. Andersen (by invitation), New York.

This paper will be published in full in a later issue of the American Journal of Diseases of Children.

CREATINE METABOLISM IN HYPOTHYROIDISM AND IN DWARFISM. DR. LAWSON WILKINS, DR. W. BLOCK (by invitation) and DR. E. LANSBERG (by invitation), Baltimore.

One of us (L. W.) has previously pointed out that marked degrees of osseous retardation may occur in dwarfs who present no evidence of hypothyroidism and who do not respond specifically to thyroid medication. Since measurement of the basal metabolic rate in children is unreliable, the study of the creatine excretion and of the blood cholesterol level was undertaken in the hope of diagnosing more accurately the thyroid factor.

Studies of the creatine excretion were made during administration of diets adequate in calories and protein but low in creatine, containing no meat or fish. The daily excretion of creatine and creatinine was determined during a control period without treatment. Observations were then made on the effect of small doses of thyroid (¼ and ½ grain [0.015 and 0.03 Gm.]) and of larger doses (2 and 3 grains [0.13 and 0.19 Gm.]). The cholesterol level was determined during the same periods. In some of the cases the creatine and the cholesterol response to the administration of a pituitary extract containing the thyrotropic hormone (prepared by Ayerst, McKenna and Harrison) were studied. These observations were made on (1) cretins, (2) hypothyroid dwarfs of classic type who responded specifically to thyroid therapy, (3) dwarfs of other types who had no features of hypothyroidism and (4) normal children.

1. Before treatment the level of spontaneous creatinuria or of blood cholesterol did not always distinguish between the cretins or the subjects with juvenile hypothyroidism and the various other types of dwarfs, nor did it differentiate them from normal children.

2. A marked increase in the creatine excretion and a sharp decrease in the blood cholesterol occurred in all the cases of cretinism or of hypothyroidism on the administration of small doses of thyroid. These marked responses usually did not occur in the other cases of dwarfism studied.

3. The creatine and cholesterol responses usually occurred much earlier than the increase in the basal metabolic rate, constituting a more delicate measurement of thyroid response.

4. In the control children the threshold dose of thyroid which caused a creatine response varied considerably, but some children responded to comparatively small doses. This may have been influenced by the fact that these were orthopedic patients, some of whom were undergoing some muscular atrophy.

In the hope of distinguishing between primary hypothyroidism and that secondary to pituitary insufficiency, biologic assays of the urine were made for the thyrotropic factor. The results were all negative with the exception of those for 1 dwarf, who has not responded therapeutically to thyroid.

The effect of the administration of a pituitary extract containing the thyrotropic hormone on the creatine excretion and on the level of blood cholesterol was studied in a number of cases. Normal children invariably showed a creatine and cholesterol response to the administration of the extract. A hypothyroid dwarf showed complete absence of response to this extract and marked response to small doses of thyroid. Various other dwarfs, some of whom were of the classic pituitary type, showed marked response to the pituitary extract, which was similar to that of the normal subjects, and showed only slight, if any, response to thyroid.

It is concluded that in cases of clearcut primary hypothyroidism there is absence of response to a pituitary extract containing the thyrotropic factor and marked response to small doses of thyroid. There are still no definite criteria to make the diagnosis of hypopituitarism. Likewise, the vexing question of the possible existence of mild, borderline degrees of thyroid insufficiency still remains unsolved.

DR. CHARLES G. KERLEY, New York: I should like to ask Dr. Wilkins his experience as to the relation of the bone age and the chronologic age of children who show delay in statural growth and somatic development.

One often sees children in whom there is a spread of several years: Thus some boys of 12 or 13 years or older will show a bone age of but 9 or 10 years, with corresponding retarded development, while children in whom the osseous retardation and defective growth resemble those encountered in the cretin show a lesser degree of retardation.

My associates and I have had satisfactory response to controlled thyroid therapy in such children, the therapy being controlled by repeated determinations of the basal metabolic rate, the blood pressure and the response of the nervous system. Our basal tests are carried out in a manner which makes the procedure available to the great majority of patients after the seventh or eighth year.

In cases of this type an assessment of the osseous development of the wrist, knee and ankle is made at regular intervals, and the child is kept under close clinical observation for several years.

I have used thyroid medication for a vast number of ill conditioned children throughout the years, and the response is often dramatically favorable.

Hypothyroidism in the child may be indicated by a wide range of developmental manifestations, and he does not have to be a cretin to demonstrate this fact.

DR. SAMUEL Z. LEVINE, New York: A few observations on the spontaneous creatinuria of infants and the effect of thyroid medication might be of interest. Normal infants excrete creatine spontaneously. If one gives them thyroid their output of creatine increases; so I think Dr. Wilkins should not be surprised to find that occurring in normal children. It is well to remember that the administration of thyroid can produce an increase in output of creatine. Surprisingly, premature infants usually do not excrete creatine, and when one gives them thyroid one cannot produce creatinuria. Dr. Gordon has demonstrated that the basal metabolic rate of premature infants is normal on the basis of surface area. This additional evidence seems to indicate that premature infants are not hypothyroid; they do not react as normal or as hypothyroid persons. When one gives thyroid to a cretin, who is not excreting creatin, creatinuria usually appears.

DR. LAWSON WILKINS, Baltimore: I am glad that Dr. Kerley talked about the significance of bone age. I took up the subject last year, and I think it is important. In recent years endocrinologists have put all the emphasis on retardation of the bone age and have claimed it to be specific of hypothyroidism. Shelton has not made that statement so boldly, but many of his followers have interpreted their findings along that line. Recently some workers in New Jersey made roentgenograms of 500 delinquent boys and studied their basal metabolic rates and blood cholesterol levels. It was found that 10.5 per cent of these children had retarded bone age without other evidences of hypothyroidism; so the investigators said that these boys were hypothyroid and that the basal metabolic rates and cholesterol levels mean nothing. We do not believe that retardation of osseous development alone is diagnostic of hypothyroidism. We have found all kinds of dwarfs who have marked delay in the bone age. I think, however, that the finding of epiphysial dysgenesis, as described by Reilly and Smyth, is of considerable significance in the diagnosis of hypothyroidism. We have never seen that in conditions which were not hypothyroid, but we have seen retarded bone age in many other types of dwarfs. Some of the slender symmetric dwarfs who had retarded bone age have been treated intensively with thyroid—to the point of hyperthyroidism—without showing any striking therapeutic response in growth, in osseous development or in biochemical change.

Dr. Levine pointed out that I should not have been surprised to find that the normal children showed marked increase in the creatine excretion with comparatively small doses of thyroid. The only reason I was surprised was that I was led astray by the fact that we had studied previously 2 or 3 normal patients and a number of dwarfs who showed little sensitivity to thyroid. In this respect they apparently resembled the premature babies referred to by Dr. Levine. I do not think we can draw conclusions yet, and I think a great deal more study must be made before we know the significance of this fact. It would be of great diagnostic importance if one could demonstrate marked sensitivity to thyroid in the hypothyroid patient and lack of sensitivity in the patient with normal thyroid function.

Second Session

Thursday Evening, May 5

MACROCYTIC ANEMIA WITH HOOKWORM INFECTION; A PRELIMINARY REPORT. DR. THOMAS E. BUCKMAN, Jacksonville, Fla.

It is generally stated in the literature that prolonged infection with hookworm causes severe anemia of the so-called secondary type, with the hemoglobin content diminished proportionately more than the number of erythrocytes. That is, the anemia of uncinariasis is not of the macrocytic variety. There can be no doubt that hypochromic anemia is associated wtih severe uncinariasis almost as a rule, and it is probably true that, as usually assumed, such anemia is due to loss of blood.

During the past three years I have had the opportunity of observing 3 cases of uncinariasis in children in whom the anemia was of the macrocytic type. Results of examinations of the blood in 2 of these cases are here presented.

In each case, the color count ratio and the volume index indicated macrocytosis, and examination of stained blood films revealed a preponderance of large red cells well filled with hemoglobin. There were few microcytes, and changes in the shapes of the cells were not marked. Moreover, the absence of polychromasia and the diminished percentage of reticulocytes suggested hypoplasia.

No causes for the anemia other than the uncinariasis could be found. Other than marked pallor and apathy, physical examination gave no unusual findings. After treatment for the parasitic condition and the administration of liver extract the anemia rapidly improved, the character of the marrow response being not unlike that observed in pernicious anemia at the onset of a remission.

In view of previously reported instances of anemia in children which simulated pernicious anemia and was not caused by intestinal parasites, no inferences can be drawn regarding the mechanism by which anemia was produced in the cases here reported. It is proposed, however, to reinvestigate the problem of anemia in hookworm infection of children, supplementing this work by studies on adults, for whom gastroscopic examinations can be made.

DISCUSSION

DR. THOMAS B. COOLEY, Detroit: I have naturally not had any large series of cases of this anemia. In one interesting family there were several cases of severe infection which differed from Dr. Buckman's in that microcytosis rather than macrocytosis was observed. Repeated finding of occult blood in the stools satisfied my associates and me that the anemia was due to chronic loss of blood, and we were not able to get any response to iron and liver therapy until we had got rid of the parasites. A curious observation was the almost complete lack of reticulocyte response during convalescence.

DR. FRANK C. NEFF, Kansas City, Kansas: I should like to ask Dr. Buckman how common this disease is in his state and if the clinical appearance of the patient suggests the disease.

DR. THOMAS E. BUCKMAN, Jacksonville, Fla.: I was much interested in Dr. Cooley's statements. Of course, that is the usual finding with hookworm anemia, and the only point in presenting these data was that our findings were unusual. Whether I shall see more of such instances I do not know, but I think the question is worth looking into.

Infection with hookworm is extremely common in Florida. Some years ago in one of the school districts most of the children were not being promoted. These children were said to have a low intelligence quotient. Of course, the parents did not like this, so they sought medical advice. The physicians suggested that the stools be examined in place of the head, and it was found that about 86 per cent of the children were suffering from hookworm infection. After adequate treatment the children regained their intelligence. I should say that in Florida hookworm infection is the commonest cause of severe anemia in children.

HYPOPLASTIC ANEMIA. DR. L. K. DIAMOND and DR. K. D. BLACKFAN, Boston.

Aplastic anemia is a disease characterized by profound progressive anemia, little or no splenomegaly, occasionally obstinate bleeding and often a fatal outcome. The blood picture is usually one of great depletion of all the elements derived from the marrow, with no signs of regeneration. There is no evidence of abnormal destruction of blood, and the circulating blood cells are relatively mature in type.

This description fits the classic case of aplastic anemia in infants and children. When, as most commonly occurs, this state is associated with severe infection or follows sepsis or toxemia, the aplastic condition may be only temporary and may improve after one or more transfusions of blood. Of such instances one sees many examples. The so-called idiopathic, more severe form of aplastic anemia, which fails to benefit materially from transfusion, is usually incompatible with the maintenance of even fair health or growth and ordinarily terminates in death, is fortunately extremely rare.

In the past seven years we have had the opportunity to see an intermediate type of anemia—hypoplastic rather than completely aplastic. This condition has been characterized by slowly progressive anemia beginning early in infancy, without any hemorrhagic tendency, with only moderate leukopenia and with the production of a small and inadequate number of reticulocytes from bone marrow which shows moderate hypoplasia.

We have studied and are reporting today 4 cases of this anemia. By means of blood transfusions given as often as necessary, the intervals between them being six to twelve weeks, the patients have been kept in relatively good health, and, contrary to the usual experience with severe anemia in this age group, they have grown and developed normally.

A typical example is the following case: K. H., an only child, of Irish-American parentage, had no family background of anemia. She was brought to the hospital at the age of 10 weeks because of gradually developing pallor of two weeks' duration. The mother's health had been good throughout pregnancy, and the child had been well fed to the time of entry. Physical examination showed an extremely pale, waxy white infant. There was slight enlargement of the heart, with a loud systolic murmur audible over the base; the liver was palpable 2 fingerbreadths below the costal margin. All laboratory examinations were negative except for the profound anemia, which was measured by an erythrocyte level of 580,000 per cubic millimeter and a hemoglobin content of about 10 per cent or 1.5 Gm. per hundred cubic centimeters of blood. The leukocytes numbered 5,000 and the platelets 110,000 per cubic millimeter. The differential smears showed no immature cells, a normal percentage of the various types of leukocytes and normal-appearing erythrocytes but less than 0.5 per cent reticulocytes. The mean cell diameter, mean corpuscular volume and hemoglobin content per cell were normal. There was no increase in the fragility of the erythrocytes in hypotonic saline solutions, and none of the usual evidences of increased destruction of blood was noted. After two transfusions the patient appeared much improved, and she was discharged in good condition.

Two months later the infant returned to the hospital because of the gradual development of pallor, which became extreme just before readmission. At this entry the erythrocyte level was 1,600,000 per cubic millimeter, and the reticulocytes were still less than 1 per cent. There were no other new findings in either physical or laboratory examinations. Oral and parenteral administration of iron in large doses as well as liver failed to effect any change in the blood. Two transfusions were given within ten days, and the patient was discharged again.

Since this time, this child has been admitted fifty-five times in all. The total number of transfusions has reached one hundred and thirteen, and the amount of blood injected to date has been about 26,000 cc.

In an effort to stimulate hemopoiesis we have used in turn pentnucleotide given intramuscularly, iron with cobalt and iron with copper given by mouth, bone marrow and spleen extract administered orally, a diet high in protein and in vitamins, and vitamin C given both by mouth and intravenously. None of these

has produced any increase in reticulocytes or improvement in the blood. Biopsy of bone marrow repeated at intervals has shown a hypoplastic state but not complete aplasia. The growth and development of the patient have been normal in comparison with those of the average child of her age.

Roentgenograms of the chest, abdomen, intestinal tract and extremities have shown no abnormality other than a moderate degree of cardiac enlargement consistent with the chronic and severe anemia. Over the last three years there has been some enlargement in the size of the liver. The spleen has not been palpable, except recently after transfusions. Gastric analysis has shown normal amounts of hydrochloric acid and a good response to a test meal.

Four patients with this syndrome have been studied. In addition, we have had an opportunity to see 2 children from other clinics. One of these, who has been followed by Dr. Rosenthal of New York at the Mount Sinai Hospital for four years, has been given transfusions repeatedly at intervals of about two months. The other patient has had a somewhat similar course under the care of the physicians at the Babies' Hospital in New York. We have heard of 2 other similar cases, 1 in California and 1 in Texas.

The outstanding features seem to be chronic progressive anemia involving mostly the erythrocytic elements. The leukocytes and platelets tend to be below the normal average in number but are not as depressed as in the severe acute aplastic anemia. The bone marrow shows no marked paucity in leukocytic centers or in megakaryocytes. There is a moderately hypoplastic state of erythrogenic elements, but no other abnormalities of growth or metabolism have so far been discovered in these children. Transfusions have been the only form of treatment effective in raising the levels of erythrocytes, although all known methods of hemopoiesis have been tried.

The infused blood generally has maintained the patient for about one or two months; then the gradual wearing out of the cells has necessitated readmission and transfusions.

Despite this frequently recurring state of profound anemia, the patients have continued to grow and develop normally in every respect.

One patient has made a complete spontaneous recovery after two years of supervision and treatment. This child now maintains an erythrocyte level of about 3,500,000 per cubic millimeter with no tendency to improve beyond this, despite the usual hemopoietic stimulants. The most recent patient of this group, a girl, was subjected to splenectomy at the age of 16 months. There was no striking change following this operation until two months ago, when the fall in erythrocytes unexpectedly was found to have stopped at about the level of 2,000,000 per cubic millimeter. No further decline has occurred over the past eight weeks. Following intramuscular administration of liver extract there has been a reticulocytosis of 6 per cent. The erythrocyte level has risen slightly. At present, therefore, the condition of the girl seems to be in a state of remission, which may become permanent if it duplicates that in the previous case.

The etiology of this condition remains obscure. No evidence of infection or of endogenous or exogenous toxemia has been discovered. To call the condition the result of aregenerative bone marrow does not seem of particular assistance in explaining it. Two theories have been entertained. First, there may be congenital insufficiency of red marrow tissue and inability on the part of the hemopoietic system to respond to the need for more blood as the erythrocytes wear out. Only the infusion of normal mature erythrocytes sustains life. With the knowledge that with the growth of the child relative concentration and diminution in the total amount of marrow tissue occur, it has been hoped that eventually the amount of hemopoietic tissue may suffice for the person's needs.

Second and more likely, an inborn error in the metabolism of some important blood-building substance may have produced a deficiency state which has led to anemia. This theory has recently been advanced and supported by the new and as yet unconfirmed investigations of Rhoads and his co-workers at the Rockefeller Institute. They have surmised the existence of an abnormality in the metabolism

of the blood porphyrins, which leads to a toxic aplastic state of the bone marrow. If this theory can be confirmed in the patients of the type reported by us, it may lead to the conception of a new congenital metabolic disturbance involving pigment substances, comparable to errors in the metabolism of carbohydrates, fats and proteins.

The investigation of our cases along these lines may be profitable. In the meantime it seems worth while calling attention to the form of hypoplastic anemia which fails to respond to the usual blood-building substances. Failure to give transfusions to these patients with sufficient frequency may well result in a fatal outcome. Transfusions administered as often as necessary may permit normal growth and development, and a spontaneous remission may occur which allows the patient to maintain the functional levels of the blood satisfactorily without assistance. At the present time the question as to the beneficial effect of splenectomy remains purely speculative.

DISCUSSION

Dr. Hugh W. Josephs, Baltimore: This condition has waited a long time for a description. Several years ago I observed 2 cases, and at that time I could find nothing in the literature which was at all similar. In 1 of these cases there were no reticulocytes at any time; in the other a few were seen after a transfusion; but, as in Dr. Diamond's case, no form of stimulation was of any effect on formation of blood. There are one or two characteristics that distinguish the condition in these cases from other types of aplastic anemia: 1. The aplasia affects the red cells only. 2. The condition is apparently present from birth. 3. There are no fluctuations in severity. In my 2 cases, when transfusions were withheld the red cells tended to fall without limit. The patients had been kept alive, one for a year and a half and the other for four years and a half, by means of transfusion every six weeks. They eventually were sent home, and they died as a result of failure to give the transfusions. From Dr. Diamond's experience there seems to be some hope that eventually if the treatment is kept up these patients may acquire some ability to make red cells for themselves. It is not unlikely that the condition is more common than might be gathered from the lack of literature on the subject. It is only lately that aplastic anemia of the newborn has been recognized. If these patients had not received transfusions shortly after birth, they would have died in the newborn period, and the condition would have been classified as anemia of the newborn, possibly without recognition of the aplastic nature of the condition. It seems likely that with the increasing interest in anemia of the newborn we shall be seeing more of this disease.

Dr. Thomas B. Cooley, Detroit: I suppose that all pediatricians encounter this condition once in a while; Dr. Diamond seems to have had an unusual number of cases; I am glad that he has brought the subject up because I believe the condition to be a real entity, though its essential nature is not yet known. It would seem to be congenital, due to incomplete development of the hemopoietic system or possibly to a metabolic defect. A somewhat similar condition occasionally seen in an older child is probably of different origin and more likely to be temporary.

It may as well be admitted that there is no therapy which really stimulates hemopoiesis in patients with these states. Occasionally, as Dr. Diamond reports, the hemopoietic system seems to take up its function after a greater or less period of time, but this is a natural process, and all the physician contributes is to keep the patient alive by transfusion.

Dr. Alfred H. Washburn, Denver: What I have to say is not altogether in line with Dr. Diamond's paper, yet I am anxious to make a plea. I wish that those of you who have contact with small, reasonably healthy, normal infants from birth on would study the blood more carefully than has been done. I am convinced that the clue to some of these conditions lies in a better understanding of the processes which are responsible for the readjustment that goes on in the early weeks of life.

In this chart the curves represent weekly examinations of the blood of 2 apparently healthy infants. I want to point out this red cell count of 2,000,000, the drop in the hematocrit reading and the dramatic curve of the reticulocytes in the

same baby. Of course, if I had given liver extract at this point the subsequent findings would have been a lovely illustration of the results one would like to get from such a procedure. I stress the fact that physicians do not have a reliable stimulant for formation of red cells, but these babies have a good one. I appeal for an attempt to get sight of the factor or factors which enable a healthy young baby to recover from severe anemia by itself. If one knew what is responsible for that sharp rise in reticulocytes, one would have an invaluable clue.

Dr. Henry J. Gerstenberger, Cleveland: During December 1935 1 of my monkeys presenting rather marked alopecia also had severe anemia. For the former condition retroflavin was administered; to my surprise this was followed in three or four days by an enormous outpouring of reticulocytes, nucleated red cells and megaloblasts, which indicated that this member of the vitamin B_2 complex probably is concerned in production of blood. Recently Gyorgy, Robscheit-Robbins and Whipple have found that retroflavin increases the production of hemoglobin in the anemic dog.

Dr. Rustin McIntosh, New York: It is obvious that the limitation of time has prevented Dr. Diamond from bringing out all the points he wanted to. Perhaps I might mention one or two in relation to a comparable patient whom my associates and I have observed. In contrast to his patients, the boy, whom we have seen for about nine years, is not making satisfactory mental and physical progress. Were it not for Dr. Diamond's experiences, we might criticize ourselves for not keeping our patient's hemoglobin level up to a more nearly normal value; but apparently his retardation is something that is peculiar to him and not to his disease. In common with many other children who have chronic anemia, these patients tend to maintain a fairly low hemoglobin concentration, to which they become adjusted. They are not appreciably more comfortable or happy when their hemoglobin is pushed up by more frequent transfusion, and it seems better to let them find their own level, which is convenient and practical. At that level they are comfortable and have good activity.

Another point of great interest is that these patients are not strikingly susceptible to infections. I think that our patient has not had any serious infection. It is true that Dr. Diamond's third patient had one, but in the group as a whole the number and severity of such episodes does not exceed what one might expect for normal subjects of comparable age. Physicians have become accustomed to feel that anemia is a handicap in a child who is trying to overcome an infection; but it is possible that their reasoning is wrong. The child has anemia because he has an infection or for the same reason that he is susceptible to infection, and the presence of anemia does not make him any more susceptible.

Dr. Louis K. Diamond, Boston: In presenting these cases we have hoped to bring to light instances of this anemia which may have been observed by some of the members here present and to receive suggestions as to the possible cause and treatment.

As has been suggested, it is indeed surprising that these highly anemic children are not more susceptible to infection, as are patients with other forms of severe anemia. In fact, these 4 patients have had much less infection than would ordinarily be expected in normal healthy children of the same age group. One of them contracted a severe Streptococcus haemolyticus septicemia following an injury to the arm by a laundry wringer and recovered satisfactorily and rapidly.

It is also interesting to note the low levels of hemoglobin to which these patients may adjust themselves without showing any diminution in activity and in appetite and without any evident embarrassment of the heart or anoxemia. Likewise, both physical and mental growth have continued unabated despite the low levels of erythrocytes and hemoglobin which are continually recurring.

Experimental Infection in the Mouse Produced by Intratracheal Inoculation with Haemophilus Pertussis. Dr. William L. Bradford, Rochester, N. Y.

By intratracheal inoculation of mice with suspensions of recently isolated Haemophilus pertussis, definite lesions of the lung were produced. The technic

consisted of exposing the trachea of the anesthetized animal and injecting 0.05 cc. of a saline suspension of the organism containing approximately 10,000,000,000 organisms per cubic centimeter. Inoculated mice became ill within twenty-four hours, and about 65 per cent of them died within ten days.

On anatomic examination the lungs were edematous and hemorrhagic and revealed focal and generalized areas of pneumonic consolidation. On section the early lesions revealed an excess of mucoid exudate within the smaller bronchi and alveolar spaces, polymorphonuclear and mononuclear cuffing about the vessels and the bronchi and in places irregular distortion of the proliferated bronchial epithelium. Bacterial stains revealed numerous clumps of organisms clustered about the surface and between the epithelial cells of the bronchi. In early lesions organisms were demonstrated in the alveolar walls and spaces throughout the lungs. In older lesions were observed typical interstitial changes, with obliteration of many alveolar spaces and distortion of others. Inclusion bodies were not noted.

Cultures of material from the lungs frequently yielded pure strains of H. pertussis as long as twenty days after inoculation. In some animals a marked degree of leukocytosis resulted.

The experimental disease, though not specific, affords an easily available method of comparing the virulence of various strains of H. pertussis and of studying the protective action of various immunizing substances.

DISCUSSION

DR. JOHN A. TOOMEY, Cleveland: I should like to ask Dr. Bradford if the virulence of H. pertussis was enhanced by the passage of organisms from mouse to mouse and if he stained those clumps to which he refers. Did he tease them loose, and, if so, were the organisms coccoid or bacillary in form?

DR. JAMES D. TRASK, New Haven, Conn.: Dr. Culotta has found that mononuclear perivascular cuffing was a prominent feature of the pulmonary histopathologic changes of whooping cough. I should like to ask Dr. Bradford if this has been his experience. I should like to ask the assembly if any one has seen a newborn baby contract whooping cough when its mother was immune to the disease.

DR. CHARLES H. SMITH, New York: I have been much interested today in three papers that presented sections of pulmonary lesions, and I cannot resist the temptation to speak about bronchopneumonia. I noted that the character of the lesion shown in the slides was that of bronchopneumonia, but not one of these speakers brought out the essential nature of the lesion. The last speaker mentioned the leukocytes between the epithelial cells as being a characteristic lesion of whooping cough, but these are merely migrating from blood vessels to the lumens of the bronchi, i. e., demonstrating endobronchitis. He did not point out that in that same section there was round cell infiltration of the submucosa, the true lesion of bronchopneumonia. Dr. Kramer and Dr. Andersen also failed to bring out the essential features of the lesions shown in their slides. In the early reactions which Dr. Bradford illustrated merely acute exudative pneumonia is present, of course.

In true bronchopneumonia there is an exudation of white cells which pours a purulent secretion into the bronchus, and there is also round cell infiltration of the submucosa. Whether the round cells come from the blood stream or arise by multiplication of tissue cells is not certain. I think that failure to recognize the essential character of the double lesion is to miss the essence of bronchopneumonia. It is present in many of the sections shown today, especially in the late lesions.

DR. WILLIAM L. BRADFORD, Rochester, N. Y.: In reply to Dr. Toomey's first question, my co-workers and I believe that the virulence of the organism may be somewhat increased by passage from mouse to mouse; certainly it is not diminished. However, we have not thoroughly investigated this point.

In view of Dr. Toomey's recent interest in morphologic changes in the organisms in relation to the various stages of the disease in children, it is only natural

that he should inquire concerning any change in the form of the organism that might occur during the course of the experimental disease in mice. So far as I know, there is none; the organism seems to retain its coccoid-bacillary form during this type of infection.

Dr. Trask's statement concerning the perivascular cuffing noted in our sections of lung is of great interest to me because the phenomenon is of frequent occurrence and because, as he stated, it is one of the conspicuous lesions commonly seen in infections due to a virus.

In regard to his question concerning maternal immunity, Dr. Lichty and I have been interested in placental transfer of antibodies in pertussis. Recent observations by Dr. Lichty in a small group of cases in a hospital would seem to indicate that the death rate from pertussis in children under the age of 6 months is higher when the mothers have not had pertussis, whereas there seems to be little correlation between the death rate in children of 6 months to 2 years of age (a period when placentally transferred antibodies would not be present) and a history of the disease in the mothers.

Dr. Smith's remarks about the peribronchial cellular infiltrates which he considered so typical of bronchopneumonia is well taken. Certainly this lesion is present in many of our sections of mouse lung. I reviewed these sections with a pathologist, who pointed out that it was difficult to state accurately the type of pneumonia which they represented. I am pleased that Dr. Smith thinks the sections shown this evening do indicate typical bronchopneumonia, because that is the type, of course, which is usually seen in the human being.

In this regard, Dr. Culotta stated that experimental lesions obtained by him in ferrets more nearly resembled the human lesion than did those obtained in mice. I have considered the lesions in the mouse to be more parenchymal than bronchial.

MECHANISM OF WHOOPING COUGH. DR. JOHN A. TOOMEY, Cleveland.

It is difficult to demonstrate the presence of pertussis toxin when freshly isolated organisms are grown on human hemoglobin blood agar. However, when small amounts of nutrient fluid are added to the solid mediums, its presence is easily shown. To preserve their virulence, organisms must be carried on 20 to 25 per cent human hemoglobin blood potato agar, the blood in the medium probably serving to keep them in that state and the starch in the potato probably providing a necessary factor for growth. In 1928, these virulent organisms were grown by me in broth cultures containing starch. They grew well, and large quantities of toxin were easily harvested. This could easily be precipitated out in the usual way by a solution of formaldehyde, sodium ricinoleate or acetic acid, a toxoid being obtained.

When organisms grown on a medium containing blood are acclimated to special slant mediums without blood and are transplanted to veal brain broth, they produce not only the endotoxic factor just referred to but a sticky exudate distinct from the toxin. The toxin produced by the organism which is freshly isolated or in the disease-producing phase of existence sensitizes the patient and causes the lymphocytosis which appears when he has finally been sensitized, at the end of the catarrhal stage of the disease. The organisms in the disease-producing state are best isolated from the patient who is in the catarrhal stage of the disease, at which time they are minute coccoid bacilli. Such organisms at that time are most virulent for guinea pigs and produce agglutinins of high titer in the blood serum of rabbits after intravenous injections. This is in decided contrast to the organisms' lessened virulence and their decreased ability to produce agglutinins in the avirulent phase of their existence.

If pertussis is caused solely by the disease-producing organisms, an antiserum made from such organisms should abort the clinical disease. If the clinical phenomena of lymphocytosis and early reactions in the disease are due to sensitization, then the use of such an antiserum should make the clinical condition worse. Serums with an agglutinin titer of 1:40,000 which had been obtained from horses and rabbits that had been inoculated with the virulent whole organisms were

injected into patients ill with the disease; they caused an increase in the number of paroxysms and whoops. Such serums did not protect guinea pigs. When antitoxin or antiserum added to bacteria or to bacterial toxin was injected intradermally in neutralization experiments, neutralization did not occur. In fact, the local reaction was greater than with antigen or antiserum alone.

It has been shown by my co-workers and me that patients with the disease gradually become more sensitive to the toxic filtrate which we have described. Thompson,* in England, this year confirmed the fact that the onset of local bacterial hypersensitiveness becomes more positive by the tenth day of the disease. Only recently Galavan and Goodpasture have stated that a toxin must be produced by the early isolated organisms to give the pathologic reactions they found.

All this may explain the mechanism of the early stage of pertussis but not that of its later stage, when the whoop starts and the patient's condition becomes clinically worse. In this stage, the virulent gram-negative coccoid bacilli become less easy to find, even though the patient is more ill, and the sticky material which causes the whoops can be easily recovered. Years ago, the cause of the disease was stated to be a mucor mycelium because stomach washings contained sporothrix-like organisms. It has been shown that such organisms do exist in pertussis, especially in the coughed up material, but they merely represent an acclimated phase in the existence of H. pertussis.

It is reasoned that patients ill with pertussis are sensitized to the virulent organisms and their toxins and become desensitized as time goes on. By the beginning of the whooping stage, the virulent organisms become acclimated and avirulent and are able to produce a by-product, the sticky mucoid material, with which all clinicians are familiar and against which it is believed the patient has to develop immunity.

We acclimated the H. pertussis organisms to various mediums, rendered them avirulent and produced in vitro the sticky mucoid secretion so characteristic of the clinical disease. Virulent organisms never produced this sticky material on blood mediums. It is believed by us that in the later stage of whooping cough antibodies are developed against this sticky product.

This year, Sprunt, Martin and McDearman produced lymphocytosis and interstitial pneumonia in monkeys and in rabbits by the intratracheal injection of H. pertussis organisms. They felt that the pneumonia was probably the result of a toxic material liberated by the organisms. They also postulated that some organisms become acclimated to the host, become avirulent and are then able to form a sticky mucoid material. They stated that they were in agreement with our theory.

It appears logical, then, to try to immunize human beings actively and passively against pertussis by the injection of the toxin and of the mucoid factor combined, as described.

Colored Motion Pictures in Teaching the Exanthems of Scarlet Fever, Erysipeloid Dermatomyositis, Measles, Indeterminable Erythema, Sulfanilamide Eruption, Chickenpox and Smallpox. Dr. D. Murray Cowie and Dr. Harry A. Towsley (by invitation), Ann Arbor, Mich.

For many years I have collected still pictures or lantern slides to illustrate to my students the various phases of the appearance of the rashes in the specific infectious fevers. The advantage of the still picture is that one can spend as much time as one wishes in discussing it. It is now possible to get excellent still pictures by color photography.

I have been fortunate to have as one of my instructors Dr. Harry A. Towsley. One of his hobbies is motion color photography. His work with flowers and the like led me to encourage him to try his luck with the rashes of contagious diseases. How well he has succeeded the members will be able to judge. His success has been due to mastering unusually well the difficult feature of illumination and, of course, to knowing exactly what we wish to illustrate. The ordinary photographer is greatly handicapped in this respect.

The length of time necessary to pose a patient for a picture is considerable. The pictures of patients with smallpox took us over three hours, and the others took an hour and a half apiece or longer. The patients with measles added the disadvantage of their sensitiveness to light.

I have used the motion color film to sum up a subject which has been presented. After a thorough description of the rash or of a series of rashes by didactic lectures and still pictures, the color movie puts on the finishing touch and illustrates the special points discussed as well, or perhaps better, than the actual patient.

It is not always possible to secure patients to illustrate lectures on the contagious diseases at the time they should routinely be presented in the course unless one has a large metropolitan hospital for contagious diseases at hand. However, in our situation usually during the course of a year enough patients are secured to illustrate most of the diseases. Smallpox is the exception. Our experience this year in particular shows the value of the color movie. The 2 patients with smallpox entered the Contagious Hospital at a time when it was impossible to get the students together. The first patient came in during vacation and the second during a week end. However, by the time the group reassembled from vacation Dr. Towsley had a film ready to show them; accordingly, they did not completely miss the case.

I find that of the large group of physicians on the staff of the University Hospital comparatively few have ever seen a patient with smallpox. One chief who had seen Dr. Towsley's pictures told me that it was the first time he had ever satisfactorily seen an enanthem in a contagious disease.

There has been difficulty in learning how to illuminate the inside of the mouth because of the interference of high light reflection. In some of the pictures of the Koplik spots, while one is able to differentiate the spots from the reflection, they are at first confusing. However, Dr. Towsley has finally overcome this difficulty.

A feature used in connection with the color movie is the loud speaker equipment, which makes it possible for the teacher to sit alongside the machine and to discuss the picture in a low, easy tone through a hand microphone as he operates the projection.

One of our pictures shows a larva in the spinal fluid of a child who was sent to the Contagious Hospital because of symptoms of involvement of the central nervous system.

Immunization Against Rabies by Vaccination with Virus Preparations Rendered Avirulent by Ultraviolet Radiation.

Dr. Horace L. Hodes (by invitation), Baltimore; Dr. Leslie T. Webster (by invitation), New York, and Dr. G. I. Lavin (by invitation), Baltimore.

A recent experimental analysis of many commercially available phenolized antirabic vaccines has thrown considerable doubt on the efficiency of these preparations and has shown that some of them contain a definite amount of virulent rabies virus. These findings are disturbing because the increasing incidence of rabies among animals constitutes a potential danger to the human population.

It seemed of importance, therefore, to produce a vaccine which would be entirely safe, yet effective when used prophylactically against rabies.

In the experiments to be described Swiss mice were employed as the test animals. A strain of virus propagated in tissue culture was employed as the source of rabies. The virulent culture virus when used as a vaccine induces good immunity in animals. But since this virulent vaccine is too dangerous for general use we attempted to develop a safe vaccine by rendering the virus nonvirulent in some way which would not destroy its immunizing potency. After we failed to accomplish this with a number of chemical agents, we tested the effect of ultraviolet radiation.

Previous investigators have shown that rabies, poliomyelitis, and other viruses are made nonvirulent by ultraviolet radiation. But all reports have indicated that viruses rendered nonvirulent in this way lose their power for immunizing animals. However, we have found that exposure to a suitable dose of ultraviolet radiation completely destroys the virulence of rabies virus, while an appreciable amount of its immunizing potency for mice is retained.

In 9 experiments the rabies culture virus was exposed to a mercury vapor lamp. The intensity of the ultraviolet radiation was estimated by means of a photronic cell and filter. Exposure to the mercury vapor lamp for thirty-five minutes or more always rendered the virus completely nonvirulent, so that it no longer produced rabies when injected into the brains of mice. However, rabies virus rendered nonvirulent by exposure for thirty-five to ninety minutes still retained an appreciable amount of its immunizing power. Vaccination with such material produced immunity in practically all mice tested against 1 minimal lethal dose of fixed rabies virus inoculated intracerebrally; it protected the great majority against 10 minimal lethal doses of virus and protected about 50 per cent against 100 minimal lethal doses. However, prolonged exposure (two hours) to the mercury vapor lamp caused the virus to lose all its immunizing power as well as its virulence.

In 3 experiments the rabies virus was rendered nonvirulent by exposure for six minutes to a mercury resonnance lamp. This nonvirulent preparation when used as a vaccine was found to protect all the mice tested against intramuscular inoculation of at least 10 minimal lethal doses of fixed rabies virus.

The technic employed in the experiments just outlined is being applied to other viruses.

DISCUSSION

Dr. James D. Trask, New Haven, Conn.: How often does the ordinary state laboratory make the diagnosis of rabies correctly? Is it safe for workers in a hospital laboratory to use mice as a test for rabies?

Dr. John A. Toomey, Cleveland: I should like to ask Dr. Hodes if he used the Flosdorf-Mudd lyophile apparatus to freeze this material and if he made any changes or additions to the medium prior to the freezing procedure.

Dr. A. A. Weech, New York: Is it not possible that the apparently greater activity of ultraviolet radiation around 2,500 angstrom units was the result of larger energy content, that is, of greater intensity of the spectral beam? The photronic cell is not so sensitive to this band of the invisible spectrum as it is to longer wavelengths, and the full dose of energy may not have been recorded.

Dr. Horace L. Hodes, Baltimore: We used the Flosdorff-Mudd apparatus to freeze and dry the rabies culture virus. The tissue culture medium contained about 10 per cent of serum, so that no more had to be added for freezing and drying. Dr. Toomey also asked about the use of broth as a diluent for the virus. We found that virus suspended in broth keeps a high titer for a longer time than in saline solution.

In answer to Dr. Weech, actually the reading on the photronic cell is lower with the spiral resonance lamp than it is when the mercury vapor lamp is used, but I think this is due to the fact that the filter transmits poorly the wavelengths of the rays given off by the spiral lamp.

In answer to Dr. Trask's question about state laboratories and a positive diagnosis of rabies, I think that Dr. Leach has shown that by using the Negri body technic alone, state laboratories probably underestimate the diagnosis by about 20 per cent. If a dog's brain is considered "negative" because microscopic examination reveals no Negri bodies, there is still a 20 per cent chance that inoculation of samples of this brain into mice will reveal the presence of rabies virus.

I believe that the mouse test is a generally safe procedure if the precautions ordinarily used for dealing with viruses are observed. Mice always have dumb rabies: they do not attempt to bite when the disease develops following inoculation.

(To be concluded)

Book Reviews

A Pediatrician in Search of Mental Hygiene. By Bronson Crothers, M.D. Price, $2.00. Pp. 271, with no illustrations. New York: Commonwealth Fund, 1938.

The title of this book is an accurate description of its contents. Dr. Crothers pictures the pediatrician as one who is uncertain of his position in the field of mental hygiene. He describes the limitation of time and the impossibility of following the procedure of the mental hygiene clinic and questions the ability of the pediatrician to treat the whole child in private practice. The pediatrician must sort out useful material contributed by the various psychiatric groups and must learn to apply it in his everyday practice. The psychologist and the psychiatric social worker are aids in the clinics and in the schools. Mental hygiene should be taught in medical schools.

Although recognizing the progress of psychiatry, pediatricians have difficulty in attempting to practice mental hygiene and at the same time to give children adequate physical care. It is difficult for the pediatrician to combine the two fields in an efficacious manner. The duties of the pediatrician, in order of importance, are: first, care of the sick child; second, physical care of the well child; third, mental hygiene of the sick and of the well child, and fourth, consideration of behavior problems. This approach should be taught to medical students and to pediatricians, who should be well trained to care for physical problems and also to "have reasonable competence in mental hygiene."

The book is well written and interesting. It is conservative, in the light of the progress that mental hygiene has made in pediatrics during the past ten years.

The Compleat Pediatrician. By Wilburt C. Davison, M.D. Second edition. Price, $3.75 (check) or $4.00 (credit). Pp. 250, with numerous tables. Durham: Duke University Press, 1938.

For the benefit of those who are not familiar with the first edition of this work, Dr. Davison states that there are 329 pediatric diseases, which may be combined into 133 groups. There are 164 symptoms and 213 laboratory tests of these conditions. These may be combined and cross indexed, so that from any given symptom the corresponding disease may be deduced. These diseases are further classified as common and uncommon, in the order of their frequency. In the new edition this system has been refined, and many sections have been revised. New methods of diagnosis and laboratory tests have been added from the newer pediatric literature, with an obviously immense amount of study and work.

I have always admired this work to such an extent that my ideas of its value may sound like a publisher's blurb. Mildly speaking, I think that it is one of the most valuable books in pediatric literature. For reference to new procedures and for stimulation in differential diagnosis, this little book is invaluable to the busy pediatrician as well as to the student.

L'administration générale de l'assistance publique à Paris. By Dr. Louis Mourier. Pp. 203, with 182 illustrations. Paris: Imprimerie Georges Lang, 1937.

Since 1849 the director of public assistance in Paris has been in charge of the administration of all hospitals for the care of the sick, the infirm and the aged, as well as the distribution of all aid furnished by public funds throughout the city.

This report covers the activity of the department of public assistance from 1920 to 1937. It includes a description of the new hospitals and of the new services developed in older hospitals. Sections are devoted to activities against venereal diseases, tuberculosis and cancer. The section on maternity and infancy deals with antepartum care, maternity hospitals, delivery in the home and the material and

instructional aid given mothers for the care of their infants. The services in children's hospitals are described. The chapter on hospital management is detailed. Other chapters discuss the measures in force for protection of the hospital personnel and the activities of social service. The numerous and well chosen illustrations show the equipment of hospitals and the operation of services.

Les huiles de foie de morue. By Paul Chabre. Price, 35 francs. Pp. 203, with 36 illustrations. Paris: Masson & Cie, 1937.

The author of this study on cod liver oils is a doctor of pharmacy. After making a few general comments on the therapeutic effects of the oil, its value in maintaining health and its economic significance, he presents the geographic distribution of the cod, types of fishing and methods of manufacturing the oil. The last part of the book has to do with the chemical constitution of cod liver oil and with methods of assaying its content of vitamins A and D. An interesting point is brought out when the oil obtained in the North Sea (Norwegian oil) is compared with that obtained off the coasts of North America and Iceland. The former, although of equal vitamin D content, is definitely inferior in vitamin A. The explanation is that the fishing season of Norway corresponds with the spawning season, when food is scarce and the liver of the fish is depleted, whereas the fishing season around North America and Iceland occurs after the spawning season, when the fish are in a good nutritional state.

The book is well written and well illustrated.

Über die körpereigene Ultraviolettstrahlung und ihre Beziehungen zur Rachitis. By Hermann Mai. Price, 9.25 marks. Pp. 81, with 4 illustrations Berlin: S. Karger, 1937.

The imaginative and experimental material of this book was inspired by the work of Gurwitsch the Russian investigator who found that certain cells in their growth emit ultraviolet rays. The author thinks that individual variation in susceptibility to rickets may depend on the individual organism's ability to produce radiation of this sort. He has devised a method of determining whether ultraviolet radiation is emitted by the blood. He finds that this phenomenon was present in most of the newborn infants studied who were born at full term but absent in the premature infants. It may be developed by treatment with sunlight or with ultraviolet radiation. According to the author, such treatment is superior to supplying vitamin D by mouth.

Tuberculosis Infantil. By Arturio Scroggie. No price given. Paper. Pp. 112, with 35 illustrations. Santiago, Chile: El Esfuerzo, 1937.

This little volume presents Dr. Scroggie's personal study of tuberculosis in the Hospital Del Rio, Santiago, Chile, of which he is chief of the pediatric section. The etiology of the disease is of interest. From a study of the source of infection of 520 children with tuberculosis, it was found that the mother was tuberculous in 44 per cent of the cases, the father in 25 per cent, brothers or sisters in 3 per cent, relatives in 6 per cent and both parents in 20 per cent.

The pathology of the various types of lesion is well illustrated by appropriate drawings and by corresponding roentgenograms of patients with typical forms. Although written in Spanish, this book will be of value to those in other countries who are interested in tuberculosis.

Child Labor and the Nation's Health. By S. Adolphus Knopf, M.D. Price, 50 cents. Pp. 32, with 7 illustrations. Boston: The Christopher Publishing House, 1937.

This brief pamphlet suggests many measures for improving the nation's health. Among these are dissemination of adequate information for birth control, supervision of venereal diseases and particularly decreasing tuberculosis through improving the health of children. The author feels that the passage of the child labor amendment is essential to prevent not only the tuberculosis that manifests

itself in childhood but that which takes its great toll in adolescent and later life. Throughout the book and in the foreword, however, he pleads especially for the creation of a ministry of public health.

Unreife und Lebensschwäche. By Dr. Albrecht Peiper. Price, 6.80 marks. Pp. 103, with 10 illustrations. Leipzig: Georg Thieme, 1937.

This concise monograph contains an excellent review of the literature pertaining to premature and weak infants, which deals with vital statistics, physical and mental growth and development, biologic chemistry and the more frequently encountered pathologic conditions.

From the standpoint of the practitioner, it is lacking in details concerning the care of the infants.

This monograph is recommended to those especially interested in a review of the literature.

The Weston-Levine Vitamin Chart. By Roe E. Remington, Ph.D., D.Sc. Seventh Revision. Price, single copy, 10 cents; 20 copies, $1.50; 50 copies, $3; 100 copies, $5; 1,000 copies, $25. Pp. 4. Charleston, S. C.: Roe E. Remington, 1937.

This chart on the vitamins takes up the names and description, the functions and the results of deficiencies. It tells where they may be found for medical use. The various foodstuffs are classified as sources of vitamins (most potent, excellent and good). The chart gives at a glance further information on vitamins.

Daily Log for Physicians. By R. F. Colwell, M.D. Price, $6. Champaign, Ill.: Colwell Publishing Company.

This is a standard account book for physicians which comes out annually, the 1938 edition being the eleventh. It is an excellent means of keeping records, not only of the usual medical items, such as daily calls and operations, but of inoculations and of the narcotics dispensed. There is also a section for figures on the social security tax. These various accounts are of much value to the physician when he figures income tax returns, budgets, etc.

The Home Treatment of Spastic Paralysis. By Percy Merritt Girard, M.D. Price, $3. Pp. 130, with 77 illustrations. Philadelphia: J. B. Lippincott Company, 1937.

This book is written for the parents of the spastic child. It explains the affliction and shows that cooperation of the parents, the physical therapeutist, the physician and the child is necessary in overcoming it. The book describes and illustrates exercises and games to help the parent in the home treatment of this condition.

Nutrition of the Infant and Child. By Julian D. Boyd, M.D. Price, $3. Pp. 198, with 40 illustrations and 12 tables. National Medical Book Co., New York, 1937.

The first chapters concern the princples of nutrition, including food requirements; following are chapters on normal diets and finally on therapeutic diets. Diabetes mellitus is dealt with in more detail then in most texts of this size, owing to the author's experience with this type of disease.

Service des enfants assistés du départment de la Seine, 1936. By Dr. Louis Mourier. No price given (government publication). Pp. 215, with 10 tables. Paris: Administration Générale De L'Assistance Publique à Paris, 1937.

After the statistical report, a detailed discussion is given of the various departments which have to do with child welfare in the department of the Seine. Hospital services, placement agencies and schools, both elementary and professional, for children depending on state care are considered. The financial report follows.

Directory of Pediatric Societies*

INTERNATIONAL

International Association of Preventive Pediatrics

President: Prof. S. Monrad, Dronning Louises Børnehospital, Copenhagen, Denmark.
Secretary: Dr. Daniel Oltramare, 15 Rue Lévrier, Geneva, Switzerland.

International Congress of Pediatrics

President: Prof. Luigi Spolverini, Policlinico Lungo Tevere Melini 24, Rome, Italy.
Secretary: Professor Vitetti, Rome, Italy.
Place: Boston. Time: Sept. 9-12, 1940.
American Committee:
Chairman: Dr. Henry F. Helmholz, Mayo Clinic, Rochester, Minn.
Secretary: Kenneth Blackfan, 300 Longwood Ave., Boston.
Canadian Committee:
Chairman: Dr. Alan Brown, Hospital for Sick Children, 67 College St., Toronto.
Secretary: Dr. H. P. Wright, 1509 Sherbrooke St., W., Montreal.

International Congress for the Protection of Infancy

Secretary: Prof. G. B. Allaria, Corso Bramante 29, Torino 120, Italy.
Place: Frankfort on the Main, Germany. Time: June 12-18, 1938.

FOREIGN

British Paediatric Association

President: Dr. Hector C. Cameron, 23 Devonshire Pl., Upper Wimpole St., London, W. 1, England.
Secretary: Dr. Arthur G. Maitland Jones, 31A Weymouth St., London, W. 1, England.

Danish Pediatric Society

President: Dr. E. Lenstrup, Copenhagen, Denmark.
Secretary: Dr. E. Gjørup, Dronning Louises Børnehospital, Copenhagen, Denmark.

Paediatrický Spolok na Slovensku

President: Dr. Pavel Radosa, Lazaretská 6, Bratislava, Czechoslovakia.
Secretary: Dr. S. Limbacher, Dlhá 2, Bratislava, Czechoslovakia.
Place: Pediatric Clinic, University, Bratislava. Time: Six times a year.

Royal Society of Medicine, Section for the Study of Disease in Children

President: Dr. E. A. Cockayne, 98 Harley St., London, W. 1, England.
Secretary: Dr. R. Lightwood, 86 Brook St., London, W. 1, England.
Place: 1 Wimpole St., London. Time: Fourth Friday of each month, 4:15 p. m.

Palestine Jewish Medical Association, Section of Physicians of Children's Diseases

President: Prof. S. Rosenbaum, 26 Bialikstr., Tel Aviv, Palestine.
Secretary: Dr. A. Brünn, 9 Maazestre, Tel Aviv, Palestine.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

Sociedad Cubana de Pediatría

President: Dr. Clemente Inclan Costa, Manrique 48, Habana, Cuba.
Secretary: Dr. Serafin Falcon Lopez, Calle B No. 356, Vedado, Habana, Cuba.
Place: Cátedra de Clinica Infantil, Hospital Mercedes, Habana. Time: Last Wednesday of every month.

Société de Pédiatrie de Paris

President: Dr. B. Weill-Hallé, 49 Avenue Raymond Poincaré, Paris.
Secretary: Dr. Jean Hallé, 10 bis Rue du Pré aux Clercs, Paris.
Place: Hôpital des Enfants Malades, 49 Rue de Sèvres, Paris. Time: 4:30 p. m., third Thursday of every month.

NATIONAL

American Medical Association, Scientific Assembly, Section on Pediatrics

Chairman: Dr. Edward Clay Mitchell, 1073 Madison Ave., Memphis, Tenn.
Secretary: Dr. Albert D. Kaiser, 16 N. Goodman St., Rochester, N. Y.
Place: St. Louis.

American Academy of Pediatrics

President: Dr. H. F. Helmholz, Mayo Clinic, Rochester, Minn.
Secretary: Dr. C. G. Grulee, 636 Church St., Evanston, Ill.
Region I. Place: Hotel Seneca, Rochester, N. Y. Time: Nov. 11-12, 1938.
Region II. Place: Skirven Hotel, Oklahoma City. Time: Nov. 16, 1938.
Region III. Place: Statler Hotel, Detroit, Mich., and Ann Arbor, Mich. Time: Oct. 27-29, 1938.

American Hospital Association, Children's Hospital Section

Chairman: Miss Mabel Binner, Children's Memorial Hospital, Chicago.
Secretary: Winifred Culbertson, Children's Convalescent Hospital, Cincinnati.

American Pediatric Society

President: Dr. Clifford G. Grulee, 636 Church St., Evanston, Ill.
Secretary-Treasurer: Dr. Hugh McCulloch, 325 N. Euclid St., St. Louis.
Place: Skytop Lodge, Skytop, Pa. Time: April 27-29, 1939.

Canadian Society for the Study of Diseases of Children

President: Dr. Alton Goldbloom, 1543 Crescent St., Montreal, Quebec.
Secretary-Treasurer: Dr. Pearl Summerfeldt, Hospital for Sick Children, Toronto, Ont.

Society for Pediatric Research

President: Dr. L. Emmett Holt Jr., Johns Hopkins Hospital, Baltimore.
Secretary: Dr. A. A. Weech, 3975 Broadway, New York.

SECTIONAL

North Pacific Pediatric Society

President: Frederick Fischer, 407 Riverside Ave., Spokane, Wash.
Secretary: Dr. C. L. Lyons, Paulsen Medical-Dental Bldg., Spokane, Wash.

Southern Medical Association, Section of Pediatrics

Chairman: Dr. Charles E. Conrad, 209-210 Professional Bldg., Harrisburg, Va.
Secretary: Dr. Hughes Kennedy Jr., Highland Plaza Apts., Birmingham, Ala.
Place: Oklahoma City. Time: Nov. 15-18, 1938.

STATE

Alabama Pediatric Society

President: Dr. Stewart H. Welch, 1117 S. 20th St., Birmingham.
Secretary-Treasurer: Dr. William R. Britton, 4 Catoma St., Montgomery.
Place: Montgomery. Time: April 17, 1939.

Arkansas State Pediatric Association

Chairman: Dr. G. D. Murphy, 112 Peach St., El Dorado.
Secretary: Dr. Madeline M. Melson, 909 Main St., Little Rock.
Place: Hot Springs. Time: January 1939.

California State Medical Society, Section on Pediatrics

Chairman: Dr. Harold K. Faber, 2341 Clay St., San Francisco.
Secretary: Dr. Hartzel H. Ray, 23–2d Ave., San Mateo.

Florida State Pediatric Society

President: Dr. Gilbert S. Osincup, 300 E. Colonial Dr., Orlando.
Secretary: Dr. Warren W. Quillian, 227 Avenue Aragon, Coral Gables.
Place: Concurrent with state association meeting at time of convention.

Georgia Pediatric Society

President: Dr. Charles Hall Farmer, 553 Walnut St., Macon.
Secretary-Treasurer: Dr. Don F. Cathcart, 478 Peachtree St., N. E., Atlanta.

Hezekiah Beardsley Pediatric Club of Connecticut

President: Dr. J. Harold Root, 103 N. Main St., Waterbury.
Secretary: Dr. Joseph L. Hetzel, 103 N. Main St., Waterbury.
Time: Three meetings a year.

Indiana State Pediatric Society

President: Dr. O. N. Torian, 23 E. Ohio St., Indianapolis.
Secretary-Treasurer: Dr. Mathew Winters, 621 Hume Mansur Bldg., Indianapolis.
Time: Two meetings a year.

Iowa Pediatric Society

President: Dr. Morgan J. Foster, 837 Higley Bldg., Cedar Rapids.
Secretary-Treasurer: Dr. Arnold M. Smythe, 406–6th Ave., Des Moines.

Louisiana State Pediatric Society

President: Dr. Ruth Aleman, 1407 S. Carrollton Ave., New Orleans.
Secretary-Treasurer: Dr. Philip C. de Verges, 312 Audubon Bldg., New Orleans.

Medical Society of State of New York, Section on Pediatrics

Chairman: Dr. Paul W. Beaven, 26 S. Goodman St., Rochester.
Secretary: Dr. Leslie O. Ashton, 842 Park Ave., New York.

Medical Society of the State of Pennsylvania, Pediatric Section

Chairman: Dr. John P. Scott, 1740 Bainbridge St., Philadelphia.
Secretary: Dr. John M. Higgins, 600 S. Wilbur Ave., Sayre.

Michigan State Medical Society, Pediatric Section

Chairman: Dr. Allan L. Richardson, 3001 W. Grand Blvd., Detroit.
Secretary: Dr. Ward L. Chadwick, 524 Medical Arts Bldg., Grand Rapids.
Place: Detroit. Time: Sept. 20-22, 1938.

Mississippi State Pediatric Society

President: Dr. Guy C. Jarratt, 920 Crawford St., Vicksburg.
Secretary-Treasurer: Dr. Harvey F. Garrison Jr., 315 E. Capitol Pl., Jackson.
Place: To be designated by Society. Time: Yearly.

Nebraska Pediatric Society

President: Dr. J. A. Henske, 1614 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. J. H. Murphy, 915 Medical Arts Bldg., Omaha.
Place: As announced by committee. Time: Third Thursday of each month from October to June, inclusive. Dinner at 6 p. m.

North Carolina Pediatric Society

President: Dr. John LaBruce Ward, Arcade Bldg., Asheville.
Secretary: Dr. Lewis Elias, 36 Grove St., Asheville.

Oklahoma State Pediatric Society

President: Dr. A. L. Salomon, 1200 N. Walker St., Oklahoma City.
Secretary: Dr. Ben H. Nicholson, 301 W. 12th St., Oklahoma City.

South Carolina Pediatric Society

President: Dr. Mylnor W. Beach, 126 Meeting St., Charleston.
Secretary-Treasurer: Dr. D. Lesesne Smith Jr., 187 Oakland Ave., Spartanburg.

Tennessee State Pediatric Society

President: Dr. William E. Van Order, 546 McCallie Ave., Chattanooga.
Secretary: Dr. Kinsey M. Buck, 1193 Madison Ave., Memphis.
Place: Jackson. Time: April 11, 1939.

Texas Pediatric Society

President: Dr. F. O. Calaway, 3306 Fannin St., Houston.
Secretary-Treasurer: Dr. F. H. Lancaster, 4409 Fannin St., Houston.
Place: Houston. Time: May 9, 1939.

Virginia Pediatric Society

President: Dr. W. Ambrose McGee, 616 W. Grace St., Richmond.
Secretary: Dr. John M. Bishop, Medical Arts Bldg., Roanoke.
Place: Danville, Va. Time: October 1938.

West Virginia State Medical Society, Section on Pediatrics

President: Dr. J. L. Blanton, 207 Fairmont Ave., Fairmont.
Secretary: Dr. Theresa O. Snaith, 450 Center Ave., Weston.

LOCAL

Academy of Medicine of Cleveland, Pediatric Section

Chairman: Dr. N. C. Wetzel, 2103 Adelbert Rd., Cleveland.
Secretary: Dr. Fred Rittenger, 10515 Carnegie Ave., Cleveland.
Place: Cleveland Medical Library Bldg. Time: October, December, February and April.

Academy of Medicine, Toronto, Section of Pediatrics

President: Dr. T. B. Verner, 170 St. George St., Toronto.
Secretary: Dr. D. V. Hutton, 170 St. George St., Toronto.

Bronx Pediatric Society

President: Dr. Samuel Tripler, 1555 Grand Concourse, New York.
Secretary: Dr. Harry S. Altman, 940 Grand Concourse, New York.
Place: Concourse Plaza Hotel, 161st St. and Grand Concourse. Time: Every second Wednesday of each month, except June, July, August and September.

Brooklyn Academy of Pediatrics

President: Dr. Benjamin Kramer, 6 Pierrepont St., Brooklyn.
Secretary: Dr. John A. Monfort, 861 Carroll St., Brooklyn.
Place: Kings County Medical Society Bldg. Time: Fourth Wednesday of each month, except May, June, July, August and September.

Central New York Pediatric Club

President: Dr. Frank Vasder Bogert, 111 Union St., Schenectady.
Secretary: Dr. Frank J. Williams, 58 S. Swan St., Albany.
Place: Various cities in New York. Time: Third Thursday of April and September.

Chicago Pediatric Society

President: Dr. Joseph K. Calvin, 2376 E. 71st St., Chicago.
Secretary: Dr. George F. Munns, 723 Elm St., Winnetka, Ill.
Place: Children's Memorial Hospital, 710 Fullerton Ave., Chicago. Time: Third Tuesday of each month, October to May, inclusive.

Dallas Pediatric Society

President: Dr. W. H. Bradford, 1719 Pacific Ave., Dallas, Texas.
Secretary-Treasurer: Dr. John E. Ashby, 3622 Fairmont Ave., Dallas, Texas.
Place: Bradford Baby Hospital. Time: 1 p. m., second and fourth Saturdays of each month.

Detroit Pediatric Society

President: Dr. William O'Donnell, 1553 Woodward Ave., Detroit.
Secretary: Dr. Robert Mason, 5140 Second Blvd., Detroit.
Place: Wayne County Medical Society. Time: 8:30 p. m., first Wednesday of each month from October to June, inclusive.

Fulton County Medical Society, Pediatric Section (Atlanta, Ga.)

Chairman: Dr. L. H. Goldsmith, 384 Peachtree St., N. E., Atlanta.
Secretary: Dr. James P. Hanner, 384 Peachtree St., N. E., Atlanta.
Place: Academy of Medicine, 38 Prescott St., N. E. Time: Second Thursday of each month from October to April, 8 p. m.

Houston Pediatric Society

President: Dr. Walter F. Qualtrough, 920 Westheimer Ave., Houston, Texas.
Secretary-Treasurer: Dr. Allan Penny Bloxsom, 4402 Travis St., Houston, Texas.
Place: Houston Club. Time: Third Monday of each month.

Intermountain Pediatric Society

President: Dr. Eugene Smith, 385–24th St., Ogden, Utah.
Secretary-Treasurer: Dr. W. C. Cheney, 1020 Boston Bldg., Salt Lake City, Utah.
Place: Salt Lake City General Hospital. Time: First Thursday of each month, 8 p. m.

Kansas City (Missouri) Pediatric Society

President: Dr. W. R. Moore, 620 Francis St., St. Joseph, Mo.
Secretary: Dr. F. S. Hogue, 1103 Grand Ave., Kansas City, Mo.
Place: Kansas City General Hospital. Time: On call.

Los Angeles County Medical Association, Pediatric Section

President: Dr. H. R. Cooder, 3875 Wilshire Blvd., Los Angeles.
Secretary-Treasurer: Dr. Paul M. Hamilton, 248 E. Main St., Alhambra, Calif..
Place: Los Angeles County Medical Headquarters, 1925 Wilshire Blvd.
Time: Second Monday of February, April, June, October and December.

Medical Society of the County of Kings and the Academy of Medicine of Brooklyn, Pediatric Section

President: Dr. Sidney D. Kramer, 61 Eastern Parkway, Brooklyn.
Secretary: Dr. Benjamin Stoloff, 1149 Eastern Parkway, Brooklyn.
Place: 1313 Bedford Ave., Brooklyn. Time: Third Wednesday of each month, October to May.

Medical Society of the County of Queens, Inc., Section on Pediatrics

Chairman: Dr. James Dobbins, 42-04 Ditmars Blvd., Long Island City, N. Y.
Secretary-Treasurer: Dr. Edith A. Mittell, 144-38th Ave., Flushing, N. Y.
Place: Queens County Medical Bldg., Forest Hills, N. Y. Time: Third Monday of October, January, March and May.

Memphis Pediatric Society

President: Dr. Barton Etter, 376 S. Bellevue St., Memphis, Tenn.
Secretary-Treasurer: Dr. Harry Jacobson, 1193 Madison Ave., Memphis, Tenn.
Place: John Gaston Hospital. Time: Quarterly.

Milwaukee Pediatric Society

President: Dr. Joseph Shimpa, 2309 N. 36th St., Milwaukee.
Secretary: Dr. Helen Jane Zillmer, 781 N. Jefferson St., Milwaukee.
Place: Children's Hospital. Time: Second Wednesday of each alternate month, beginning with February.

New England Pediatric Society

President: Dr. Hyman Green, 483 Beacon St., Boston.
Secretary-Treasurer: Dr. Henry E. Gallup, 1101 Beacon St., Brookline, Mass.
Place: Boston Medical Library. Time: Four meetings a year, occurring from September to May.

New York Academy of Medicine, Section of Pediatrics

Chairman: Dr. Philip M. Stimson, 25 Claremont Ave., New York.
Secretary: Dr. Lucy Porter Sutton, 168 E. 74th St., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: Second Thursday of each month from October to May, inclusive, 8:30 p. m.

Northwestern Pediatric Society

President: Dr. Roger L. J. Kennedy, Mayo Clinic, Rochester, Minn.
Secretary-Treasurer: Dr. Robert Rosenthal, 437 Lowry Medical Arts Bldg., St. Paul.
Place: Minneapolis, St. Paul, Duluth and Rochester. Time: January, April, July and October.

Oklahoma City Pediatric Society

President: Dr. A. L. Salomon, 1200 N. Walker St., Oklahoma City.
Secretary: Dr. G. R. Felts, 1200 N. Walker St., Oklahoma City.
Time: Every month, except June, July and August.

Philadelphia Pediatric Society

President: Dr. Julian M. Lyon, 40 Llanfair Rd., Ardmore, Pa.
Secretary: Dr. Aims C. McGuinness, Children's Hospital, 1740 Bainbridge St., Philadelphia.
Place: College of Physicians, 19 S. 22d St. Time: Second Tuesday of each month from October to April, inclusive.

Pittsburgh Pediatric Society

President: Dr. James LeRoy Foster, Highland Bldg., Pittsburgh.
Secretary-Treasurer: Dr. E. R. McClusky, 3200–5th Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine. Time: Second Friday, alternate months from October to June, inclusive.

Richmond Pediatric Society

President: Dr. A. S. Hurt, 1028 W. Franklin St., Richmond, Va.
Secretary-Treasurer: Dr. Louise Fry Galvin, 2416 Stuart Ave., Richmond, Va.
Place: Richmond Academy of Medicine, 1200 E. Clay St. Time: First Thursday of each month (except July, August and September).

Rochester Pediatric Society

President: Dr. J. Merrel Parker, 11 N. Goodman St., Rochester, N. Y.
Secretary: Dr. H. C. Soule, 16 N. Goodman St., Rochester, N. Y.
Place: Arranged by program committee. Time: Second Friday of each month.

Rocky Mountain Pediatric Society

President: Dr. John Schoonover, Republic Bldg., Denver.
Secretary: Dr. F. Craig Johnson, 1850 Gilpin St., Denver.
Place: Children's Hospital, Denver. Time: First Saturday of each month from September to May, inclusive, 7:30 p. m.

St. Louis Pediatric Society

President: Dr. John Zahorsky, 536 N. Taylor Ave., St. Louis.
Secretary-Treasurer: Dr. Max Deutch, 634 N. Grand Blvd., St. Louis.
Place: St. Louis Medical Society. Time: Third Friday of every month.

Seattle Pediatric Society

President: Dr. Walter B. Seelye, 1305–4th Ave., Seattle.
Secretary: Dr. Armin Rembe, 1215–4th Ave., Seattle.
Place: College Club. Time: Third Friday of each month, 6:30 p. m.

Southwestern Pediatric Society

President: Dr. Philip E. Rothman, 3875 Wilshire Blvd., Los Angeles.
Secretary: Dr. Norman Nixon, 1136 W. 6th St., Los Angeles.
Place: University Club of Los Angeles. Time: First Wednesday in January, March, May, September and November.

University of Michigan Pediatric and Infectious Disease Society

President: Dr. Damon O. Walthall, 1103 Grand Ave., Kansas City, Mo.
Secretary: Dr. D. Murray Cowie, University of Michigan, Ann Arbor, Mich.

Westchester County Medical Society, Pediatric Section (New York)

President: Dr. Norman Survis, 650 Main St., New Rochelle, N. Y.
Secretary-Treasurer: Dr. Elvira Ostlund, 131 Purchase St., Rye, N. Y.
Place: Grasslands Hospital, Valhalla, N. Y. Time: Third Thursday in October, December, February and April.